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(71)(72) Applicants and Inventors: BECKER, Robert, O. [US/US]; Erie Canal Road, P.O. Box 278, Lowville, NY 13367 (US). KANIA, Bruce, G. [US/US]; P.O. Box 5186, Bozeman, MT 59717 (US).

(74) Agent: REICHMANIS, Maria; P.O. Box 3306, Aiken, SC 29802 (US).

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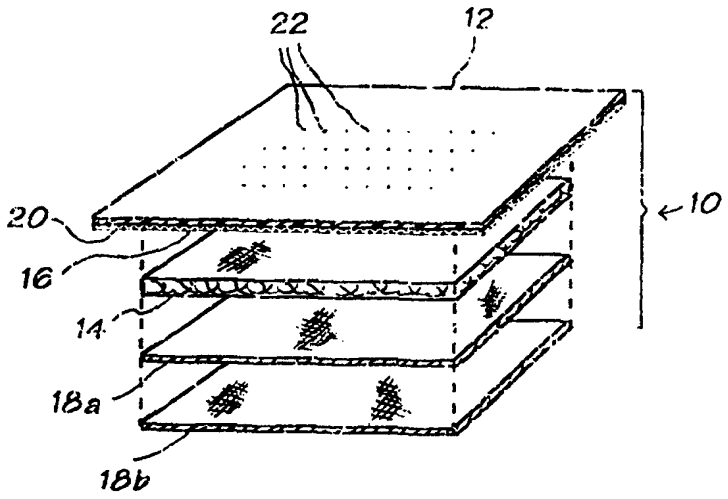
(54) Title: MULTILAYER ANTIBACTERIAL TREATMENT DEVICE

(57) Abstract

A multilayered antimicrobial device (10) for therapeutic and prophylactic use, including a first layer (18) consisting of at least one sheet of flexible, conformable, bactericidal fabric. Additional layers may include a moisture–absorbing material (14) adjacent the bactericidal fabric, and a thin, flexible outer layer (12) of moisture–impermeable material. To minimize the use of adhesives and fixatives, the edges of these layers are preferably bonded together by heat/pressure bonding techniques. The silver is attached to the fabric substrate of layer (18) in a mechanically stable form that releases small quantities of ionic silver when wetted. Device (10) can be used for prophylactic and therapeutic care and treatment of skin infections, surface wounds, surgical incisions, as a wound packing material, and as an adjuvant to conventional deodorants. Device (10) is made of nontoxic, nonhazardous, non–irritative, nonallergenic materials, and is inert until activated by contact with water, perspiration or other suitable liquid.



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MULTILAYER ANTIBACTERIAL TREATMENT DEVICE

TECHNICAL FIELD OF THE INVENTION

The present invention relates to multilayer devices having physiologically beneficial antimicrobial, antifungal, and antiviral properties. In particular, the present invention relates to silver-containing devices for use as wound packing materials, as dressings for the care and treatment of surface wounds, and as deodorizing inserts in socks, stump socks, athletic shoes, sole and heel pads, garment shields, and the like.

BACKGROUND ART

The care and treatment of wounds is an important part of health care, incorporating the sometimes-irreconcilable goals of satisfactory outcomes, responsiveness to patient concerns, and cost-effectiveness. Wound healing is a cellular process which is triggered by the occurrence of an injury (as used herein, the terms "wound" and "injury" refer to tissue damage or loss of any kind, including but not limited to cuts, incisions (including surgical incisions), abrasions, lacerations, fractures, contusions, burns, amputations, and so forth). Healing is believed to be controlled by a biophysiological feedback mechanism that monitors the extent of the injury and controls cellular activity in the injured area to produce the types and numbers of cells needed to accomplish a repair.

Many conditions can interfere with normal healing processes, including impaired circulation, conditions such as diabetes and infections at the situs of the injury which frequently result in non-healing or slowly-healing wounds, unfavorable outcomes, and increased health care costs. In response to these concerns, many hospitals have established specialized centers to treat non-healing wounds. A wide variety of treatment modalities, including local and systemic antibiotics, antibiotic-impregnated dressings, antibiotic and antifungal compositions, and the like are available for treating infected wounds, slowly-healing wounds, and non-healing wounds. Many of these are used prophylactically in an attempt to forestall infections, which are a growing concern due to the spread of antibiotic-resistant strains of bacteria.

Silver and other metals have been widely used in antimicrobial and antifungal applications (for purposes of this detailed description, a metal with "antibiotic," "antimicrobial," "cidal," "bactericidal" and/or "bacteristatic" properties is broadly defined as a metal that is active against at least one pathogenic microorganism, including but not limited to bacteria, protozoa, fungi, rickettsiae, and viruses. Bactericidal agents kill microorganisms, whereas bacteristatic agents prevent their growth and multiplication). Topical preparations that contain silver or silver compounds—silver nitrate, silver sulfadiazine, colloidal silver

compositions, silver-protein compounds such as Argyrol™, and so forth—are widely used in medicine. For example, ointments containing silver sulfadiazine are widely used for the treatment of infected burns.

Modern applications of silver date from Crede's technique of using dilute silver nitrate solution as prophylaxis of gonorrhea opthalmicum in newborn infants. The first modern recorded use of silver in surgery was in 1913, when Halsted reported the successful use of silver foil as the initial dressing for fresh surgical incisions. In the same paper, Halsted advocated the use of rubber gloves and rubber tube surgical drains, both of which were immediately accepted by the surgical community and which, in updated forms, are still in use today. For unknown reasons the use of silver foil never quite became popular.

The introduction of natural and synthetic antibiotics in the 1940s revolutionized the treatment of systemic bacterial infections such as pneumonia and septicemia. However, the direct use of antibiotics in localized, infected wounds proved to be unsatisfactory due to their irritative and allergic effects on human tissues. As a result, such infections are frequently treated with systemic administration of antibiotics. Now, however, the nature of infectious processes has been greatly changed with the spread of antibiotic-resistant strains, the prevalence of mixed infections, and the dearth of new antibiotics. As a result, effective treatment of local infections has become much more difficult, requiring systemic administration of large doses of multiple antibiotics often with attendant undesirable side effects.

Even after the introduction of antibiotics, infections of bone (i.e., osteomyelitis) remained difficult to treat because the limited blood supply to this tissue precluded obtaining adequate local levels of systemically administered antibiotics. The appearance of mixed and antibiotic-resistant infections has further complicated this situation. Even today, the only effective treatment for osteomyelitis remains primarily surgical, and includes adequate wound débridement, leaving the wound open during healing, and supplementing with appropriate systemic antibiotics.

The effectiveness of silver as an antimicrobial agent is at least partly determined by the delivery system. Most silver compounds that dissociate readily yield cations that are highly toxic to human tissues, and therefore are not considered suitable for medical use. Less-toxic compounds, including silver sulfadiazine cream (widely used in the treatment of burns) and silver nitrate solution, do not dissociate readily. These topical compounds must therefore be re-applied frequently to maintain their clinical efficacy.

Iontophoretic (i.e., electrically-generated) silver ions, which can penetrate more deeply into the tissues than silver ions from topical compounds, have been found to inhibit bacterial and fungal growth in vivo and in vitro at current densities as low as 10 nA/mm^2. Silver ions are effective even against antibiotic-resistant strains of bacteria and fungi. Iontophoretic silver treatment is somewhat more effective than treatment with silver compounds, with generally the same spectrum of activity as that of silver nylon. The effects

of electrically-generated silver ions are described in a number of publications, including the following: J. A. Spadaro, et al., "Antibacterial Effects of Silver Electrodes with Weak Direct Current," Antimicrobial Agents & Chemotherapy, Vol. 6, pp. 637-642 (1974); T. J. Berger, et al., "Antifungal Properties of Electrically Generated Metallic Ions," Antimicrobial Agents & Chemotherapy, Vol. 10, pp. 856-860 (1976); R. O. Becker, et al., "Treatment of Orthopedic Infections With Electrically-Generated Silver Ions," J. Bone & Joint Surgery, Vol. 60-A, pp. 871-881 (1978)).

Silver and other metals are used in a number of wound dressings, in the form of pure metal, metal salts, or other compounds. For example, McKnight, et al. disclose a laminated collagen dressing for treating burn (U.S. Patent No. 3,800,792). Their dressing is made from a layer of reconstituted collagen film laminated to a thin continuous layer of an inert polymer material such as polyurethane. The collagen film may contain finely divided silver metal particles, added by soaking the dried film in Tollen's reagent to oxidize excess glutaraldehyde and deposit silver metal on the accessible surfaces of the collagen fibers.

Weaver, et al. show a disposable, multilayer electrode that includes a nonconductive cover sheet, a nonmetallic, conductive disperser sheet (preferably made of carbon-containing silicon rubber), and a non-adhering wound contact sheet (U.S. Patent No. 5,218,973). This device is designed to prevent migration of metal ions into the wound being treated. Fabo (U.S. Patent No. 5,340,363) discloses a dressing that includes an outer absorbent layer and an inner porous, hydrophobic layer knitted of elastic threads and encapsulated by a soft, hydrophobic silicone or polyurethane gel. The gel can be used as a carrier for antibacterial agents such as zinc, pain-relieving substances, and agents that stimulate wound repair. Klippel, et al. use micronized allantoin as a carrier for a bactericidal or bacteristatic ingredient (such as silver citro allantoinate) that is dispersed on the surface of a plastic air splint or other bandaging product (U.S. Patent No. 3,830,908).

Stowasser makes a dressing of absorbent, metal-coated fibers, such as carding fleece coated with aluminum and backed by compressed cellulose, and polyamide fibers coated with vacuum-deposited silver (U.S. Patent No. 2,934,066). Matson (U.S. Patent No. 4,728,323) coats a substrate (nylon fabric, polymeric film, fiberglass, gauze or polyurethane foam) with a film of a silver salt deposited by vapor or sputter coating techniques. Alternatively, fibers can be coated and then woven or knitted into a fabric. Konikoff (U.S. Patent No. 4,142,521) shows a bandage or surgical sponge material incorporating one or more electret elements, each electret providing a small electrostatic field to the area of the wound.

Dressings for provision of electrical stimulation are also known. For example, Rogozinski (U.S. Patent No. 5,395,398) discloses a composite dressing that includes an elliptical or circular pad with a pure silver anode surrounded by a ring of base metal, a dorsal support layer, surface contact layers of electrically-conductive hydrogel polymer, and two battery-powered generators. Silver, et al. provide a wound dressing made of biocompatible, biodegradable collagen sponge with carbon or metal (including silver) electrodes inserted

therein (U.S. Patent No. 4,703,108). The electrodes do not release metallic ions into the wound, and are removed surgically once the wound heals. D'Alerta's patch includes an electronic circuit for delivering a pulsed stimulus, circuitry including a cathode and an anode, a double-sided adhesive layer, a top layer which seals the circuit layer from moisture, and a backing layer (U.S. Patent No. 5,423,874).

Jones (U.S. Patent No. 4,911,688) covers a wound with a clear cover that serves as a hollow chamber for holding a fluid such as saline in contact with a wound. When connected to a voltage source, a metal anode and a return electrode create free ions and an electrical field to enhance healing and tissue regeneration. Juhasz (U.S. Patent No. 4,817,594) discloses a multi-layer dressing for covering discharging, malodorous wounds. The dressing includes a layer of an electrically-conductive material such as silver and a layer of charcoal fabric. Application of a DC (direct current) voltage to the conductive layer drives silver ions into the wound to enhance tissue growth and inhibit bacterial growth; application of transcutaneous AC (alternating current) is used for post-operative pain relief. Seiderman (U.S. Patent No. 4,767,401) describes a bandage-like device used for iontophoretic administration of medicaments, including silver-protein colloids. The device includes a metal foil electrode (preferably aluminum), and makes use of the slight inherent negative electric charge proximate a wound site to generate a small electric field at the site.

In applications Serial Nos. 08/623,046, filed March 28, 1996 and 08/969,935, filed 11/28/97, Becker, et al. disclose a silver-containing wound dressing and a bimetallic fabric having large numbers of contact junctions between two dissimilar metals, respectively. In a preferred embodiment, the junctions of the bimetallic fabric are formed between a first metal (such as silver) and a second metal (such as gold or platinum). When the fabric is contacted with an electrolyte, each such bimetallic junction acts generates free silver ions. The disclosures of the above-referenced patent applications are incorporated herein by reference.

An iontophoretic system for promoting tissue healing processes and inducing regeneration is described in U.S. Patent No. 5,814,094, the disclosure of which is incorporated herein by reference. The system is implemented by placing a flexible, silver-containing anode in contact with the wound, placing a cathode on intact skin near the anode, and applying a wound-specific DC voltage between the anode and the cathode. Electrically-generated silver ions from the anode penetrate into the adjacent tissues and undergo a sequence of reactions leading to formation of a silver-collagen complex. This complex acts as a biological inducer to cause the formation in vivo of an adequate blastema to support regeneration.

Regardless of whether silver is provided in the form of silver ions, silver metal or a topical composition such as silver nitrate solution or silver sulfadiazine cream, its beneficial effects are believed to be limited by the achievable local concentration of silver ions. Certainly, these effects are manifested primarily at the contact surface and immediately adjacent tissues.

Another widespread concern relates to objectionable body odors, both normal odors and those arising from infections, metabolic disorders, and syndromes that give rise to profuse, malodorous perspiration. Despite the almost-universal rise in standards of personal and public hygiene during this century, objectionable body odors are still a problem for many people. Body odor is largely due to bacterial action in fluid secretions, particularly perspiration. Almost all mammals, including humans, have sweat glands (also termed sudoriferous glands): small, tubular glands found almost everywhere on the body, but which are especially numerous in the armpits and on the palms and soles. The sweat glands play an important role in regulating body temperature: these glands secrete moisture, which evaporates, cools the body surface, and helps maintain normal body temperature.

Human perspiration is also believed to contain hormonal end products and pheromones that may serve as sexual attractants: Napoleon I is said to have written Josephine from the battlefield, telling her he was on the way home and asking her not to wash. On the other hand , most people dislike the odor of stale perspiration. Odor is not merely a personal or a social concern: more importantly from a medical standpoint, distinctive odors may signal the presence of pathological conditions. For example, infected wounds frequently smell bad compared to clean, uncontaminated wounds (prior to the advent of penicillin and other antibiotics, military physicians were all too familiar with the smell of gangrenous wounds).

The feet are a major source of objectionable odors. Even though the soles contain large numbers of sweat glands, perspiration odor from the feet is not particularly noticeable when going barefoot or wearing sandals. However, feet encased in shoes, with or without hose or socks, quickly develop a distinctive "locker-room" odor which most people perceive as unpleasant. Odors of this nature are an especial concern to amputees, who typically wear close-fitting tubular socks over a residuum to help cushion a prosthesis.

People have approached the problem of masking or eliminating objectionable body odors in many different ways. Perfumes in almost infinite variety, in the form of oils, colognes, tinctures, lotions, powders, and soaps, have been used since antiquity. Deodorant soap became popular in this century, as did the use of underarm deodorants and antiperspirants (for purposes of this specification, deodorants are defined as substances that are applied to the skin to mask, reduce, or suppress body odors; antiperspirants are preparations, usually containing astringents, applied to the skin to decrease perspiration). Dress or garment shields are worn to protect the underarm areas of clothing from stains caused by perspiration.

Whatever their origin, objectionable body odors are a source of embarrassment and discomfort to large numbers of people. Deodorants and antiperspirants are helpful in masking or reducing odors due to underarm perspiration, and dress shields protect clothing by absorbing perspiration. However, many people cannot use common deodorants and antiperspirants due to allergies. Furthermore, presently-available deodorants and antiperspirants do little to alleviate locker-room odor due to bacterial growth.

Despite the availability of a variety of wound dressings, delivery systems (both passive and iontophoretic) for supplying bactericidal metals such as silver to a wound, and numerous deodorant and antiperspirant compositions, there is an unmet need for a simple, versatile, cost-effective device that is capable of supplying useful amounts of silver in a variety of applications.

DISCLOSURE OF THE INVENTION

According to its major aspects and broadly stated, the present invention is a multilayered antimicrobial device for therapeutic and prophylactic use. The device includes a first layer consisting of at least one sheet of a flexible, conformable, bactericidal fabric. Additional layers may include at least one sheet of moisture-absorbing material adjacent the bactericidal fabric, a moisture reservoir, and, optionally, a thin, flexible outer layer of moisture-impermeable material that serves as an occlusive barrier to direct moisture (wound exudates, perspiration, etc.) to the target area. To minimize the use of adhesives and fixatives, the edges of these layers are preferably bonded together by heat/pressure bonding techniques known in the art.

The bactericidal fabric contains a metal such as silver that is effective against a broad spectrum of microorganisms, including but not limited to sepsis-causing bacteria and odor-causing bacteria. (For purposes of this detailed description, a metal with "antimicrobial," "bactericidal" and/or "bacteristatic" properties is broadly defined as a metal that is active against at least one pathogenic agent, including but not limited to bacteria, protozoa, fungi, rickettsiae, and viruses. Bactericidal agents kill organisms, whereas bacteristatic agents prevent their growth and multiplication.) The silver (or other bactericidal metal) is preferably in a mechanically stable form that remains bound to the fabric substrate when dry, but that releases useful amounts of silver ions when moistened by a liquid such as water, saline solution, wound exudate, perspiration, and so forth. Thus, when the device contacts the target area, at least a portion of the silver contained therein is eventually released into the surrounding tissues with resulting beneficial effects. The device itself is durable, nontoxic, nonhazardous, substantially nonallergenic and nonirritating, and inert until activated by contact with a suitable liquid (water, perspiration, wound exudate, hydrocolloid, etc.).

When used in the care and treatment of skin infections, ulcers, surface wounds (including surgical incisions) and the like, a device according to the present invention is effective in slowing the growth of microorganisms such as bacteria and fungi in the treated area. The device also provides an effective prophylactic measure against airborne contaminants and opportunistic infections. When installed inside a shoe, sock, stump sock, pantyhose, or shoe, the device is activated upon hydration with perspiration (if desired, the device may be pre-moistened with water or other suitable liquid prior to use). In this application, the device is effective in slowing the growth of odor-causing bacteria that thrive

in the relatively warm, relatively moist environment of shod feet, thereby slowing the onset of perceptible locker-room odor.

An important feature of the present invention is the bactericidal fabric, which contains a bactericidal/bacteristatic metal (preferably silver) on a flexible, conformable, moisture-absorbing, nonallergenic, non-adhering fabric substrate. For consumer appeal, the fabric may also have a good "hand" and an esthetically-pleasing appearance. The bactericidal fabric may be sufficiently thick that it acts as a stent, that is, it can retain moisture and is capable of seeping up wound exudates. To avoid or minimize the use of adhesives, fixatives, and so forth, the edges of the sheets (and of the absorbent layer, if present) are preferably bonded together by heat/pressure bonding techniques known in the art. Suitable silver-containing fabrics for the invention include felted, loop, matted, pile, tricot, warp knit, and other silver nylon fabrics. In a preferred embodiment of the invention, the bactericidal fabric contains at least approximately 2 wt.% silver, more preferably at least approximately 10–15 wt.% silver; however fabrics with silver contents outside these ranges may also be useful.

Another feature of the present invention is the provision of at least two sheets of bactericidal fabric in the form of a layered or laminar structure, each sheet having a useful metal content. In the case of silver, useful fabrics generally contain at least approximately 2 wt.% silver. Fabrics that contain more silver by weight are generally believed to have more available silver for treatment purposes than those that contain less silver, whether the additional silver is in the form of a thicker coating, a greater admixture of silver-coated fibers, or smaller-diameter fibers that provide a larger silver-coated surface area. However, those skilled in the art recognize that there is a practical upper limit to the amount of silver that can be deposited on any type of fabric, due to the difficulty of producing mechanically stable silver deposits on fabric. No matter what the manufacturing technique, fabrics with silver contents greater than approximately 20 wt.% tend to be mechanically unstable, in that the silver deposits are subject to flaking and powdering so that the silver is easily lost when handling the fabric and the ability of the coating to release biologically-effective silver ions is diminished. Thus, the delivery of silver ions to the treatment site has heretofore been limited (at least in part) by the achievable silver content of these fabrics. These types of fabrics are not suitable for use with the present invention, which requires a mechanically stable silver-containing fabric wherein the silver is transferred via oligodynamic action.

Provision of two or more layers of silver-containing fabric in the present invention is predicated upon the surprising discovery that these are as effective as a single layer with approximately the same silver content—even where the single layer contains the same amount of silver as the two layers combined. That is, two layers provide substantially the same amount of silver ions at the treatment site as a single layer having twice the silver content by weight. Each sheet contains a biologically-effective amount of mechanically-stable silver on a flexible, conformable, non-adhering fabric substrate such as nylon. Thus, a treatment device with two or more silver-containing sheets delivers more useful silver ions to the treated area,

without the disadvantages of powdering and flaking associated with fabrics having higher silver contents. With a sufficiently large number of silver-containing sheets, however, the overall flexibility of the device and the added amount of free silver ions per additional sheet tend to decrease.

Still another feature of the present invention is the absorbent layer of the device, which, if present, is made of a moisture-absorbing material of sufficient thickness to serve as a stent. The moisture-absorbing material seeps up wound exudates, maintains the moist condition of the wound, and furthers migration of silver ions to the treatment site. Suitable materials include soft, flexible, conformable fabrics made of natural fibers such as cotton, synthetics such as polyester, rayon, dacron, polyurethane, acrylic and modacrylic, thermoplastics, and so forth. In one embodiment of the invention, this layer may itself contain silver or other bactericidal metal, for example, at least approximately 2 wt.% silver and more preferably at least approximately 5–10 wt.% silver.

Yet another feature of the present invention is the moisture-impermeable layer, which serves as an occlusive barrier that helps entrain fluids and direct them to the bactericidal fabric. In a preferred embodiment, the moisture-impermeable layer is also gas-permeable to further ventilation of the treated area. Suitable materials include Goretex® and the types of plastics used in Band-Aid® type dressings.

Another feature of the present invention is its versatility. The treatment device may consist simply of one or more sheets of silver-containing fabric that, when moistened by any suitable liquid (including but not limited to water, wound exudates, and perspiration), release silver ions that act to slow the growth of microorganisms at the treated site. A device of this type is useful as a wound dressing or wound packing material; it may also be used prophylactically to slow the growth of odor-causing bacteria in socks, stump socks, shoes, garment shields, etc. This type of device may also include a sheet of some fabric that is capable of absorbing at least some moisture. In another embodiment of the invention, the device includes, in sequence, a sheet of moisture-impermeable, gas-permeable material such as Goretex®, a sheet of moisture-absorbing material, and one or more sheets of silver-containing fabric, the combination being sufficiently flexible to conform generally to the area being treated. A treatment device according to the invention can be dimensioned according to the intended use; it can be made by any convenient techniques known in the art, of readily available, generally inexpensive materials. It can be provided in a convenient form for a variety of applications, ranging from prepackaged, presterilized individual units such as BandAid®-type dressings to rolls or sheets that can be cut to size as needed. The device can be applied to surface wounds such as cuts (including surgical incisions), scrapes, and burns. It can also be applied to intact skin to treat localized infections. In still another embodiment of the invention, the device includes a connector for making electrical contact with a power source used for iontophoretic treatment.

Other features and advantages of the present invention will be apparent to those skilled in the art from a careful reading of the Best Modes for Carrying Out the Invention presented below and accompanied by the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings,

Figs. 1A–1C show the results of in vitro tests of several silver-containing products;

Fig. 2 is an exploded, perspective view of a wound treatment device according to the present invention;

Fig. 3A is a cross-sectional view of the device of Fig. 1;

Figs. 3B and 3C are detail, cross-sectional views of additional embodiments of a device according to the present invention;

Fig. 4 is a plan view of a finger-tip dressing according to the present invention;

Figs. 5A and 5B are cross-sectional views of wound packing materials according to a preferred embodiment of the present invention;

Fig. 6A is a perspective view of another wound packing material according to a preferred embodiment of the present invention;

Fig. 6B is a perspective view of a dispenser for a wound packing material according to the invention;

Fig. 7A is a perspective view of a deodorizing insert according to a preferred embodiment of the present invention;

Fig. 7B is a cross-sectional view of the insert of Fig. 7A;

Fig. 7C is a cross-sectional view of another deodorizing product according to the invention;

Figs. 8A and 8B are cross-sectional views of iontophoretic treatment devices according to the present invention;

Figs. 9A and 9B are perspective views of additional devices according to the present invention; and

Fig. 9C is a detail, cross-sectional view of the fastener of the device of Fig. 9B.

BEST MODES FOR CARRYING OUT THE INVENTION

In the following description of best modes for carrying out the invention, reference numerals are used to identify structural elements, portions of elements, surfaces or areas in the drawings, as such elements, portions, surfaces or areas may be further described or explained by the entire written specification. For consistency, whenever the same numeral is used in different drawings, it indicates the same element, portion, surface or area as when first used. Unless otherwise indicated, the drawings are intended to be read together with the specification, and are to be considered a portion of the entire written description of this

invention as required by 35 U.S.C. § 112. As used herein, the terms "horizontal," "vertical," "left," right," "up," "down," as well as adjectival and adverbial derivatives thereof, refer to the relative orientation of the illustrated structure as the particular drawing figure faces the reader.

The effectiveness of silver against several strains of wound sepsis and odor-causing bacteria was tested in vitro using five silver-containing fabrics. The bacteria tested included standard bacterial strains obtained from the American Type Culture Collection ("ATTC") and multiply drug-resistant ("MDR") clinical isolates ("CI") obtained from the Burn Trauma Intensive Care Unit of the University of Utah Medical Center. Of the tested fabrics, Products 2 and 3 differed in that Product 2 was pre-treated by exposure to the atmosphere; Product 3 was untreated. Also tested were the Arglaes™ controlled-release film dressing (Product 6), and 1% silver sulfadiazine (Silvadine®) cream on a non-silver-impregnated nylon fabric (Omnishield, Inc.; Product 7). The silver content of an 18 mm disc of each product is listed in Table I.

Table I. Silver content of tested products.

No.	Product	Ag Content (mg/18 mm disc)
1	Omnishield, Inc. silver-impregnated warp knit fabric	3.36
2	Omnishield, Inc. silver-impregnated aged pile fabric	7.78
3	Omnishield, Inc. silver-impregnated new pile fabric	7.02
4	Swift, Inc. silver-impregnated fabric	4.84
5	Sauquoit Industries silver-impregnated fabric	11.65
6	Arglaes™ controlled-release film dressing	0.22
7	1% Silvadine® cream on Omnishield, Inc. pile fabric (w/o silver)	0.30

Eighteen-millimeter discs of each product were prepared and tested in vitro on several sepsis-causing and odor-causing bacteria according to a modified Kirby-Bauer protocol using three different test configurations (A, B, and C, as described below). Test species included Acinetobacter. (CI #s 1–4), Brevibacterium epidermidis (ATCC #35514), Corynebacteriium xerosis (ATCC #373), Enterobacter cloacae (ATCC #13047), Escherichia coli (ATCC #11229), Micrococcus lylae (ATCC #27566), Proteus mirabilis (ATCC #4630),

Pseudomonas aeruginosa (MDR) (CI #s 1 and 2), Serratia marcescens (ATCC #14756), Staphylococcus epidermidis (ATCC #12228), and Stenotrophomonas maltophilia (MDR) (CI #s 1 and 2).

Test Configuration A. Discs of Products 1–7 were tested for the ability to continue to emit silver ions with continued use. The discs were applied directly to newly-inoculated Kirby-Bauer plates filled with approximately ninety (90) mL of Mueller-Hinton Agar, and moistened with sterile 0.85% saline. Each Kirby-Bauer plate contained three disks which were treated with one of the seven products.

The plates were incubated for 48 hours, after which zones of inhibition (as measured outward from the edge of the disc) were read after 48 hours for each disc (1st microbial challenge). For purposes of these studies, the measured zone of inhibition for each disc was defined as the distance in millimeters between the edge of the disk and the outer edge of the zone of inhibition. The discs were then applied to fresh Kirby-Bauer plates inoculated with the same bacteria and incubated for an additional 48 hours, and the zones of inhibition were measured (2nd microbial challenge). This procedure was repeated a third time (3rd microbial challenge). Test results are shown in Tables II and III.

Table II. Results for Test Configuration A discs (Product 1).

No.	Microorganism	Average Zone of Inhibition (mm) 1st Microbial Challenge	2nd Microbial Challenge	3rd Microbial Challenge
1	Acinetobacter. (CI #1)	3.00	2.00	1.00
2	Acinetobacter. (CI #2)	2.50	1.00	0.50
3	Acinetobacter. (CI #3)	2.17	1.33	0.00
4	Acinetobacter. (CI #4)	2.17	1.17	0.33
5	Brevibacterium epidermidis (ATTC #35514)	2.67	1.83	0.50
6	Corynebacterium xerosis (ATTC #373)	1.17	1.67	1.67
7	Enterobacter cloacae (ATTC #13047)	0.50	0.00	0.00
8	Escherichia coli (ATTC #11229)	0.17	0.00	0.00
9	Micrococcus lylae (ATTC #27566)	3.17	2.50	1.50

10	Proteus mirabilis (ATTC #4630)	1.00	0.00	0.00
11	Pseudomonas aeruginosa (MDR) (CI #1)	3.00	2.17	0.67
12	Pseudomonas aeruginosa (MDR) (CI #2)	3.83	3.33	2.33
13	Serratia marcescens (ATTC #14756)	0.50	0.67	0.00
14	Staphylococcus epidermidis (ATTC #12228)	3.67	2.33	2.00
15	Stenotrophomonas maltophilia (MDR) (CI #1)	2.00	0.50	0.00
16	Stenotrophomonas maltophilia (MDR) (CI #2)	3.83	2.50	1.67

*measured outward from the edge of the Product
ND = no data

Table III. Representative test results for Test Configuration A discs (Products 1–7).

Microorganism	Product #	Average Zone of Inhibition (mm) 1st Microbial Challenge	2nd Microbial Challenge	3rd Microbial Challenge
Acinetobacter. (CI #1)	1	3.00	2.00	1.00
	2	3.33	4.50	2.00
	3	2.67	1.67	1.50
	4	3.00	2.50	1.50
	5	3.50	4.00	2.50
	6	1.00	0.50	0.00
	7	3.17	1.50	1.33
Brevibacterium epidermidis (ATTC #353514)	1	2.67	1.83	0.50
	2	2.83	2.33	1.00
	3	2.67	1.00	0.00
	4	2.00	2.50	1.00
	5	3.67	2.83	1.00
	6	1.17	0.00	0.00
	7	3.17	1.33	0.17
C. xerosis (ATCC #373)	1	1.17	1.67	1.67
	2	1.83	4.00	3.00
	3	8.67	4.50	1.83
	4	1.50	3.00	1.00
	5	2.33	6.00	3.00
	6	0.83	0.50	0.00
	7	1.17	1.00	0.50
Micrococcus lylae (ATTC # 27566)	1	3.17	2.50	1.50
	2	3.67	4.33	2.67
	3	5.00	3.83	2.00

		4	5.00	3.50	2.00
		5	5.67	5.33	4.50
		6	1.83	0.50	0.00
		7	5.17	3.00	1.50
	P. aeruginosa (MDR)	1	3.83	3.33	2.33
	(CI #2)	2	2.83	10.00	5.50
		3	3.50	9.67	10.50
		4	3.50	7.50	9.50
		5	4.50	7.00	9.33
		6	2.00	4.00	0.00
		7	3.67	1.67	0.00
	S. epidermidis	1	3.67	2.33	2.00
	(ATCC #12228)	2	3.67	4.67	3.50
		3	3.67	7.67	3.50
		4	3.67	3.00	3.00
		5	3.67	6.66	5.50
		6	3.67	1.00	0.50
		7	3.67	2.33	1.67

*measured outward from the edge of the Product
ND = no data

Test Configuration B. The test protocol was the same as described above for Configuration A, with the exception that the contact surfaces of discs removed from the Kirby-Bauer plates were washed with sterile 0.85% saline before placement on newly-inoculated Kirby-Bauer plates. Representative test results are shown in Table IV.

Table IV. Representative test results for Configuration B discs.

		Average Zone of Inhibition (mm)		
		1st Microbial	2nd Microbial	3rd Microbial
Microorganism	Product #	Challenge	Challenge	Challenge
Acinetobacter.	1	3.00	1.00	0.50
(CI #1)	2	3.67	2.67	1.67
	3	2.67	2.00	1.00
	4	3.00	2.00	1.00
	5	3.00	3.67	2.17
B. epidermidis	1	2.83	0.50	0.00
(ATTC #353514)	2	3.17	1.33	0.50
	3	2.83	0.50	0.00
	4	2.50	0.50	0.00
	5	3.17	1.17	0.50
C. xerosis	1	1.00	1.00	0.00
(ATCC #373)	2	2.33	3.17	1.50
	3	5.50	2.00	0.00
	4	1.50	2.50	1.00
	5	1.33	3.83	3.50
Micrococcus lylae	1	2.17	2.00	1.00
(ATTC # 27566)	2	3.00	3.83	1.50
	3	4.67	2.50	1.00

	4	5.00	3.00	1.00
	5	5.33	5.00	2.00
P. aeruginosa (MDR)	1	4.00	2.83	10.00
(CI #2)	2	3.00	10.67	6.83
	3	3.00	9.00	5.50
	4	2.00	6.00	3.00
	5	4.33	5.00	4.33
S. epidermidis	1	3.67	3.00	2.50
(ATCC #12228)	2	3.67	4.00	4.50
	3	3.67	4.00	2.83
	4	3.67	4.50	4.00
	5	3.67	6.67	5.83

*measured outward from the edge of the Product
ND = no data

Test Configuration C. The test protocol was the same as described above for Configuration A. Discs were left in place on inoculated Kirby-Bauer plates for five (5) days, and were re-moistened with saline after 72 and 96 hours (i.e., on days 3 and 4). Zones of inhibition were read every 24 hours. Test results are shown in Table V.

Table V. Representative test results for Configuration C discs.

		Average Zone of Inhibition (mm)				
		1st	2nd	3rd	4th	5th
Microorganism	Product #	Day	Day	Day	Day	Day
Acinetobacter.	1	3.17	3.00	3.83	3.50	3.00
(CI #1)	2	3.17	3.00	3.83	3.50	3.33
	3	2.50	2.83	3.33	2.67	3.00
	4	3.00	2.50	3.00	3.00	3.00
	5	3.00	3.00	3.83	3.00	3.17
	6	1.00	1.00	1.00	1.00	1.00
	7	3.00	2.33	3.17	2.67	2.50
Brevibacterium	1	3.50	3.33	2.17	2.00	1.50
epidermidis	2	3.67	3.17	2.83	2.50	2.00
(ATTC #353514)	3	3.17	2.67	1.67	2.00	1.33
	4	3.00	2.50	1.50	2.00	2.00
	5	3.67	3.33	3.17	3.00	3.00
	6	1.17	1.00	0.50	0.83	0.00
	7	3.33	2.67	2.83	3.00	2.17
C. xerosis	1	1.17	1.67	1.67	2.00	1.50
(ATCC #373)	2	2.17	2.00	2.33	3.00	1.83
	3	6.17	6.67	9.17	9.00	6.50
	4	1.00	1.50	1.00	1.00	1.00
	5	2.00	1.50	2.00	2.00	1.67
	6	0.50	0.50	0.00	0.50	0.00
	7	1.00	0.50	0.50	0.83	0.50
Micrococcus lylae	1	4.83	4.67	4.17	4.17	3 83
(ATTC # 27566)	2	5.00	4.33	4.17	4.50	4.33
	3	4.67	4.83	4.50	4.00	4.67

	4	5.00	4.50	3.50	4.00	4.00
	5	5.33	5.17	5.00	5.33	4.83
	6	2.50	1.50	1.83	1.17	0.83
	7	5.00	4.67	4.33	4.17	3.33
P. aeruginosa (MDR)	1	3.00	3.17	3.17	3.33	3.00
(CI #2)	2	2.83	3.50	3.17	3.00	3.00
	3	2.83	3.17	3.17	2.33	3.00
	4	3.00	3.00	3.00	3.00	3.00
	5	5.00	5.00	4.83	4.67	4.17
	6	1.83	1.83	2.00	2.00	2.00
	7	3.67	3.67	3.33	3.33	3.00
S. epidermidis	1	3.67	3.83	3.67	4.17	3.33
(ATCC #12228)	2	3.67	4.00	4.33	4.17	4.00
	3	3.67	4.17	5.17	6.00	4.50
	4	3.67	4.00	3.50	4.00	4.00
	5	3.67	6.00	6.17	7.00	6.67
	6	1.83	2.00	2.17	2.33	1.50
	7	4.00	4.17	4.17	4.33	3.17

*measured outward from the edge of the Product
ND = No Data

While Kirby-Bauer tests are interpreted in qualitative rather than absolutely quantitative terms, the silver-containing fabrics (Products 1–5) exhibited antimicrobial activities at least equal to that of the Silvadine® dressing (Product No. 7), and better than that of the Arglaes™ dressing (Product No. 6). Configuration C discs showed greater retention of antimicrobial activity that either Configuration A or Configuration B discs; Configuration A discs showed greater retention of antimicrobial activity than Configuration B discs. Based on these test results, it appears that factors other than silver content alone may influence the effectiveness of the tested products against various strains of bacteria.

With the exceptions noted below, Product No. 5 was the most effective in absolute terms. Despite a lower silver content, Product No. 2 had zones of inhibition similar to those of Product No. 5 for Acinetobacter. 1–4, suggesting that use of the aged pile fabric may enhance effectiveness. Effectiveness against Corynebacterium xerosis depended on the test configuration and the challenge, and none of the tested products was more than minimally effective against Enterobacter. cloacae, E. coli, and P. mirabilis.

Products 1–5 and 7 were found to be effective against odor-causing bacteria (products 2 and 3 were more effective against Corynebacterium xerosis than Products 1, 4, and 5). Surprisingly, the overall effectiveness of Product 2 (treated surface) was greater than that of Product 3 (untreated surface). These results indicate that silver-containing fabric is effective in reducing the multiplication of odor-causing bacteria *in vitro*.

A useful factor for evaluating the effectiveness of the different products across the sixteen microorganisms, three test configurations, and multiple microbial challenges within each configuration is the silver effectiveness ratio (SER), defined as follows:

SER (mm/g) = mean zone of inhibition/amount of silver in product

The SER is a relative measure of each product's effectiveness on the basis of its silver content. Figs. 4A–C are plots of the SER for Microbial Challenges 1, 3, and 5 for Test Configuration C across all 16 microorganisms. Within each plot, the tested microorganisms are generally arranged in decreasing order of product effectiveness (that is, there is a downward trend in product effectiveness when scanning from left to right).

Product 1 tended to have the largest SERs; thus, the values for this product are connected by solid lines. Any points above the line indicate a product superior to Product No. 1, having a larger SER associated with that product for that specific microorganism.

These data indicate that factors other than silver content alone may influence the effectiveness of the tested products. For example, Products 2 and 3 are notably effective against Acinetobacter. (Table IV); Products 3 and 5 are effective against the odor-causing bacterium Corynebacterium xerosis (Table IV); Products 2 and 3 are effective against Staphylococcus epidermidis (Table V).

As measured in the above-described Kirby-Bauer test protocol, none of the tested products exhibited especially good activity against the Gram-negative species tested. The antibiotic-resistant clinical isolates exhibited variable susceptibility. However, all tested products were effective against B. epidermidis, Micrococcus lylae, P. aeruginosa, and S. epidermidis. Products 1–5 and 7 were found to be effective against odor-causing bacteria, but only Products 2 and 3 were highly effective against Corynebacterium xerosis. In general, however, these results demonstrate that silver nylon fabric is an effective antimicrobial agent for use with the present invention.

In additional tests, the antimicrobial properties of a test fabric (silver-containing nylon) and a control fabric were compared when challenged with three bacterial strains, including two strains obtained from the American Type Culture Collection (Escherichia coli, ATCC # 11229; Staphyloccous epidermidis, ATCC # 12228) and a vancomycin-intermediate, methicillin-resistant strain of Staphylococcus aureus obtained from the Centers for Disease Control (CDC). The test fabric was a silver-containing nylon loop fabric manufactured by Omnishield, Inc.; the control fabric was identical save for the silver coating.

A total of eighteen 1" (about 2.5 cm) square pieces of the test and control fabrics were prepared, and each piece was placed into a sterile 50 mm x 9 mm Petri dish. A challenge suspension consisting of a 0.55 mL aliquot of approximately 1.0×10^9 CFU/mL in 50% (v/v) fetal bovine serum, prepared according to standard techniques, was inoculated onto each fabric piece; six such pieces were inoculated with each challenge suspension for each product. Airtight lids were placed onto the dishes containing the inoculated product pieces, and the dishes were incubated at 35° ± 2° C for periods of thirty minutes, four hours, and twenty-four hours.

After each period of incubation had elapsed, two pieces of each product per microorganism species were removed from the Petri dishes, placed into separate sterile bottles each containing 100 mL of Butterfield's Phosphate Buffer solution with product neutralizers, and mixed thoroughly. Four ten-fold dilutions (10^{-1}, 10^{-2}, 10^{-3}, and 10^{-4}) were made from each bottle in Butterfield's Phosphate Buffer solution, mixing thoroughly between dilutions.

Aliquots of the product-neutralizer/inoculum suspension dilutions were pour-plated, in duplicate, using Mueller-Hinton Agar. The plates were incubated for 40.75 to 41.5 hours at 35° ± 2° C. Following incubation, the colonies on the plates were counted manually using a hand-tally counter.

The Initial Population (IP) in CFU/mL, Inoculum Level (IL) in CFU/product piece and Microorganism Population (P_{EX}) in CFU/product piece were computed in absolute and Log_{10} values, and the Log_{10} Difference and % Difference of each microorganism on the product pieces were computed as follows after 30 minutes, four hours, and twenty-four hours incubation:

$$IP = ((1/n)\Sigma C_i) \times 10^{D},$$

where C_i is the individual plate count, n is the number of plates (n = 2 for this study), and D is the dilution factor of counts used;

$$IL = IP \times V_{IP},$$

where IP is the Initial Population of the challenge suspension and V_{IP} is the volume of Initial Population used to inoculate each product piece (V_{IP} = 0.5 mL in this study);

$$P_{EX} = 100\ (((1/n)\Sigma C_i) \times 10^{D}),$$

where C_i and n are defined above and D is the dilution factor of counts used;

$$Log_{10}\ Difference = Log_{10}\ IL - Log_{10}\ P_{EX},$$

where IL is the Inoculum Level per 1"-square product piece at time = 0 and P_{EX} is the population on the product pieces following incubation per exposure time; and

$$\%\ Difference = 100\ ((IL - P_{EX})/IL).$$

The results of these tests are summarized in Tables VI–VIII.

Table VI. Average Inoculum Levels (Log_{10} and CFU/product piece) for test (silver-containing nylon fabric) and control (nylon fabric) products.

Microorganism	Product	IL (Log_{10})	IL (CFU/product piece)
E. coli (ATCC # 11229)	test	8.6675	4.650×10^8
	control	8.6675	4.650×10^8

S. epidermidis (ATCC # 12228)	test	8.6075	4.050×10^8
	control	8.6075	4.050×10^8
S. aureus (CI)	test	8.7160	5.20×10^8
	control	8.7160	5.20×10^8

Table VII. Average populations after exposure (Log_{10} and CFU/product piece) for silver-containing nylon and control products for the three microorganisms tested at each of three exposure times (30 minutes, 4 hours, and 24 hours).

Microorganism	Exposure Time	Product	P_{EX} (Log_{10})	P_{EX} (CFU/ product piece)
E. coli (ATCC # 11229)	30 min.	test	8.3430	2.205×10^8
	"	control	8.5116	3.250×10^8
	4 hrs.	test	< 2.4646	< 4.750×10^2
	"	control	9.0872	1.225×10^9
	24 hrs.	test	< 2.0000	< 1.000×10^2
	"	control	9.1425	1.393×10^9
S. epidermidis (ATCC # 12228)	30 min.	test	7.6933	5.000×10^7
	"	control	8.2706	1.865×10^8
	4 hrs.	test	< 2.0000	< 1.000×10^2
	"	control	8.3298	2.163×10^8
	24 hrs.	test	< 2.0000	< 1.000×10^2
	"	control	8.5119*	3.250×10^8*
S. aureus (CI)	30 min.	test	8.4877	3.075×10^8
	"	control	8.6873	4.875×10^8
	4 hrs.	test	5.4281	2.533×10^8
	"	control	8.4017	5.200×10^8
	24 hrs.	test	< 2.0000	< 1.000×10^2
	"	control	8.0106	1.075×10^8

*Represents data from one fabric piece.

Table VIII. Log_{10} Differences and % Differences for silver-containing nylon and control products for the three microorganisms tested at each of three exposure times (30 minutes, 4 hours, and 24 hours).

Microorganism	Exposure Time	Product	Log_{10} Difference	% Difference
E. coli (ATCC # 11229)	30 min.	test	0.3245	52.581
	"	control	0.1557	30.108
	4 hrs.	test	> 6.2028	> 99.999
	"	control	0.0000	0.000
	24 hrs.	test	> 6.6675	> 99.999
	"	control	0.0000	0.000
S. epidermidis (ATCC # 12228)	30 min.	test	0.9142	87.654
	"	control	0.3370	53.9506

	4 hrs.	test	> 6.6075	> 99.999
	"	control	0.2777	46.605
	24 hrs.	test	> 6.6075	> 99.999
	"	control	0.0956*	19.751*
S. aureus (CI)	30 min.	test	0.2283	40.865
	"	control	0.0287	6.250
	4 hrs.	test	3.2879	99.943
	"	control	0.3143	51.298
	24 hrs.	test	> 6.7160	> 99.999
	"	control	0.7054	79.327

*Represents data from one fabric piece.

As indicated by the results listed in Table VII, the test product (silver-containing nylon fabric) reduced the challenge populations of all three microbial species tested as compared to the control product.

The above-described test results indicate that silver-containing fabric is effective against a broad range of microbial species, including Gram-positive and gram-negative strains, and common strains of sepsis-causing and odor-causing bacteria.

Referring now to Figs. 2 and 3A–C, there is shown a multilayer, silver-containing wound treatment device 10 according to a preferred embodiment of the present invention. Device 10 (also referred to as a "dressing" or a "wound dressing") may include a thin, flexible outer layer 12 that serves as a cover, an intermediate layer 14 of absorbent material attached to the medial portion of layer 12 by any suitable technique (for example, with an adhesive 16), and at least one inner layer 18 (preferably a laminar structure with at least two sheets 18a, 18b of silver-containing fabric) to be described further below. The edges of layer 12 may be coated with a skin-contact adhesive 20, protected with a removable strip of material (not shown) that is peeled off just prior to use.

The edges of layer 14 (if present) and sheets 18a, 18b may be attached together by any convenient technique, including but not limited to application of heat and pressure, embossing, crimping, sonic welding, needle punching, and biocompatible adhesives such as adhesive 16. However, techniques which avoid the use of adhesives, fixatives, and so forth are preferred.

Outer layer 12, if present, is preferably a sheet of electrically non-conducting, substantially water-impermeable material that aids in keeping optional intermediate layer 14 and sheets 18a, 18b moist while device 10 is in use to help promote healing. Layer 12 may also serve as an occlusive barrier that entrains fluids and directs them to silver-containing layers 18a, 18b. Layer 12 may include a plurality of perforations 22 therethrough to provide additional ventilation of the wound surface if desired. However, layer 12 is preferably a semipermeable material (air and gas-permeable but water-impermeable), that functions as a semiocclusive membrane to slow the rate of water loss. Layer 12 is preferably somewhat larger than layers 14 and 18a, 18b to permit application of adhesive 20 to the edges (Fig. 2A).

Suitable materials for layer 12 include Goretex®, vinyl, polyethylene, and plastics such as those used in many commercially-available dressings (BandAid®, Curad®, etc.).

Layer 14 is a sheet of soft, flexible, conformable, moisture-absorbent material of adequate thickness to serve as a stent, that is, a material that can retain water and is capable of seeping up wound exudates, etc. (layer 14 may be moistened with water, normal saline, or other suitable liquid prior to or during use of device 10). Suitable materials include cotton, polyester, rayon, dacron, polyurethane, polypropylene, acrylics and modacrylics, polyvinyl acetate or other synthetic materials, thermoplastic materials, or combinations thereof, in woven, nonwoven, foam, or sponge-like form. Layer 14 need be no more than approximately 0.1–0.5 cm thick for most applications; however, thicker layers may be useful when device 10 is used in the care of relatively large draining wounds in excess of 4 $in.^2$ in size or thereabouts. Materials that are at least somewhat compressible may be useful for maintaining good contact between inner layer 18 and the treated area.

As noted above, device 10 includes a inner, laminar layer having at least two adjacent sheets 18a, 18b of silver-containing material. Sheets 18a, 18b are preferably made of a substrate material that is dimensionally stable, biologically inert, easily handled whether moist or dry, substantially non-adhering (that is, the material does not normally adhere to skin, exposed tissues, etc.). The substrate material is one that maintains its structural integrity in use, that is, the substrate fibers do not easily become dissociated from sheets 18a, 18b under normal conditions (fabrics made of chopped fibers, and fabrics that "shed" or "pill" easily are generally not suitable for use with the invention). Sheets 18a, 18b, like layer 14, are at least somewhat flexible and conformable, and are made by any convenient process that produces a material with at least approximately 2 wt.% silver (preferably at least approximately 5 wt.% silver, more preferably at least approximately 15 wt.% silver). Lower silver concentrations may also be useful for some applications.

Suitable substrate materials for sheets 18a, 18b include, but are not limited to, polymers such as nylon, dacron, rayon, polyester, acrylics and modacrylics, polyamides, polyimides, polyolefins, polyphenylenes, acetates, and other natural and synthetic fibers and blends thereof. Bicomponent fibers (also known in the art as composite fibers) may also be useful where the individual layers of device 10 are to be bonded together. These types of fibers consist of two components of different melting or softening points so that, when a fibrous web of such fibers is heated to a temperature above the lower of the two softening points but below the higher softening point, one of the two components softens and bonds the fibers together.

Useful fibers may vary broadly in basis weight and structure, ranging from very fine fibers having a basis weight of less than 5 denier to coarser fibers of 50 denier or more. The substrate is preferably manufactured of biologically inert, nonconductive, nonimmunogenic fibers (since many people are sensitive to certain fibers, the substrate is preferably also nonallergenic or hypoallergenic).

The fabric substrate of sheets 18a, 18b incorporates or is coated with useful amounts of silver by any convenient technique. For example, the substrate may be a woven, knitted, or nonwoven silver-plated fabric. Alternatively, the substrate may be made of a combination of silver-coated (or silver-impregnated) and plain fibers. Suitable materials for sheets 18a, 18b include silver-impregnated warp knit nylon fabric, silver-impregnated nylon pile fabric, and other fabrics made by Omnishield, Inc., Swift, Inc., Sauquoit Industries, and other manufacturers. Other useful fabrics include polyesters, polyethylenes, rayons, acrylics, and combinations thereof that contain useful amounts of silver.

In one preferred embodiment of the present invention, layer 14 contains at least approximately 2 wt.% silver, more preferably at least approximately 5–10 wt.% silver. However, it should be noted that silver concentrations outside this range may also be useful for some applications. Suitable materials include silvered and plain nylon fabric made by Omnishield, Inc., Sauquoit Industries and other manufacturers; however, other materials may also be useful for the practice of the invention. Layers 14, 18 may be made by weaving, knitting, felting, blowing, or other convenient process.

Silver (or some other metal with medically useful properties) is added to sheets 18a, 18b (and layer 14, if desired) by vapor coating, aerosolized deposition, sputter coating, chemical deposition, plating, or other techniques known in the art. Individual fibers can be coated and then worked (woven, knitted, crocheted, felted, blown, etc.) into a fabric; alternatively, silver may be added to the finished fabric. Useful fabrics may contain as little as 5–10% or as much as 100% silver-coated fibers. While the amount of added silver may vary broadly, the fabric preferably contains enough silver so that sheets 18a, 18b have a specific resistance no greater than approximately 5 Ω/cm (more preferably, no greater than approximately 1 Ω/cm). However, fabrics with higher specific resistances (as high as 10 Ωcm or more) may also be useful. The added silver is in a highly purified form, that is, at least approximately 99.9% pure and preferably at least approximately 99.99% pure.

If layer 14 contains silver, this layer is of a material that contains at least approximately 2 wt.% silver (preferably at least approximately 5–10 wt.% silver); sheets 18a, 18b contain at least approximately 2 wt.% silver, preferably 5–15 wt.% or more. Suitable materials contain approximately 0.05–0.50 g/cm^2 silver, with layer 14 preferably having a lower silver content than sheets 18. The metal content and specific resistance of layers 14, 18, as well as the thickness and uniformity of the metal coating, may vary broadly depending on the intended uses of device 10. Materials containing less metal may be useful for some applications, as may those with higher specific resistances. However, it should be understood that the materials for layers 14, 18 are selected with a view to providing the needed amounts of free silver to the treatment site. Other metals with antibacterial and/or antifungal properties may also be useful for the practice of the present invention, including but not limited to gold, copper, aluminum, zinc, and combinations and alloys thereof.

Layers 14, 18 are not only made of materials having a sufficiently high content of silver (or other useful metal) to provide useful amounts of silver ions in vivo, but materials that have an approximately uniform distribution of silver. Non-uniform distributions may result in non-uniform treatment, since the amount of silver supplied to different areas of the target site may differ. The thickness of the silver coating on the fibers of layers 14, 18, like the basis weight of the fibers used to make the substrate, may vary broadly. Useful amounts of silver may be achieved with coatings no greater than 1 or 2 micrometers thick; however, the optimum coating thickness for any particular application depends on the basis weight and shape of the fibers, the type of fabric (i.e., knit, loop, pile, etc.), the selected metal, and the intended application.

The silver in layers 14, 18 is preferably in a form that, when device 10 is placed in contact with body tissues and moistened by a suitable liquid, releases silver ions by the passive dissolution of silver in ionic form from the metallic silver surface in a process known as oligodynamic action. Thus, over a period of time, at least a portion of the available silver migrates to the immediately-adjacent tissues where it has useful antimicrobial and antifungal effects.

While not wishing to be bound by theory, it is believed that metallized (i.e., metal-containing, metal-coated, metal-plated) materials wherein the metal atoms are firmly attached or bound to a fabric substrate when dry, but are at least somewhat releasable in ionic form when wetted with a suitable liquid, are especially suitable for the practice of the present invention. For example, layers 14, 18 may be made of materials that contain silver (or other suitable metal) in the form of small crystals which tend to release free silver ions when wetted by saline, water, wound exudate, or other suitable liquid. Crystalline silver deposits of this type are believed to have a greater effective surface area than conventional silver-plated coatings, and therefore the capability of releasing more silver ions per unit coating weight, in shorter periods of time. However, other types of silver-containing materials may also be useful.

A multilayer device according to the present invention can be manufactured in a variety of useful shapes for use in different applications or different wound sites. Device 10 could, for example, include a slit or throughhole for accommodating a drain, catheter, external fixation device, or the like. For example, a device 30 adapted for use on fingertip wounds, has a thin, flexible outer layer 12, an inner layer with at least two adjacent silvered sheets 18 (for clarity, only the lowermost such sheet is shown), and an optional layer 14 between sheets 12 and 18 (Fig. 4). A layer of adhesive 20 coats the exposed inner side of layer 12. A plurality of radial slits 32 extend inwards from the periphery of dressing 30 to form a series of flaps 34 about a central portion 36. Dressing 30 preferably has at least three or four slits 34 forming four flaps 34. However, a greater number of slits 32, such as the twelve slits 36 at approximately 30° intervals (Fig. 4), results in a better-fitting dressing.

Portion 36 is centered on the fingertip with layer 18 adjacent to the skin and covering the area to be treated. Flaps 34 are affixed to the skin proximal to the wound by adhesive 20. By overlapping flaps 34 appropriately, the user can form dressing 30 into a "cap" that covers the fingertip. While human fingers vary widely in size, a dressing 30 approximately 2" (about 5 cm) in diameter with a central portion 36 approximately 1" (about 2.5 cm) in diameter is believed to be suitable for use on most fingertip wounds. However, dressing 30 can easily be made in different sizes to better fit small or large fingertips.

Device 10 is inert until silver-containing layers 18a, 18b are wetted by any of a variety of agents: water, wound exudate, or other suitable liquid. Then, at least some free silver ions are released from layers 18a, 18b and migrate from the fabric substrate into the surrounding region. When placed so that at least one of silver-containing layers 18a, 18b contact the wound surface, naturally-occurring body fluids may be sufficient to activate this process. More frequently, device 10 is activated by moistening with a suitable liquid to promote the release of free ions. Distilled or sterile water is preferred, since tap water tends to vary in quality and frequently contains ions which interfere with the emission of silver from layers 18a, 18b. Hydrocolloid preparations such as DuoDerm™ (manufactured by Convatec) may be useful in maintaining moisture in device 10, and do not interfere with silver ion emission from the device.

The use of two sheets 18a, 18b in device 10 is predicated upon the surprising discovery that a device with two or more silver-containing sheets is more effective than one with a single sheet, since two sheets have been found to provide at least the same amount of silver ions at the treatment site as a single sheet having twice the silver content. This property results in a device 10 that delivers more silver to the treated area, without the disadvantages of powdering and flaking associated with fabrics having higher silver contents. With a sufficiently large number of silver-containing sheets, however, the overall flexibility of the device and the added amount of free silver ions per each additional sheet tend to decrease. Thus, the optimum number of sheets 18a, 18b is best determined by a modest amount of experimentation and observation for each particular application and combination of materials.

It should be noted that device 10 is self-sterilizing, that is, layers 18a, 18b sterilize themselves when wetted as a result of the antimicrobial effect of the silver contained in these layers. As a result, even though a device 10 is preferably used only once, it may be rinsed and reused whenever fresh devices are unavailable.

After device 10 is placed on a wound, silver ions are released from layers 18a, 18b into the adjacent tissues (if layer 14 contains silver, additional silver ions may also be released from layer 14). The rate of release generally rises to a maximum that depends on the silver content of the layers, then gradually decreases over a period of approximately 12–72 hours. As each silver ion leaves the fabric substrate, it is replaced by an ion from the local wound environment (i.e., chloride, etc.). In addition, some of these other ions may bind spontaneously to the remaining silver on the fabric. Thus, while layers 14, 18a, 18b still

contain silver at the end of the treatment period, some of that silver will be unavailable for treatment purposes. While device 10 may be rinsed and reused several times if desired, the device will eventually lose at least some of its antimicrobial activity.

The present invention is further illustrated by the following non-limiting examples.

EXAMPLE 1

A 45-year-old male accidentally inserted his left foot beneath a rotary lawn mower, incurring traumatic amputation of the tip of the 5th toe, the entire 4th toe at the M-P joint, and the distal half of the distal phalanx of the 1st toe including the soft tissue pad. The patient initially presented with grossly contaminated wounds which were washed, debrided, and left open with moist dressings applied. Mixed antibiotics were started after cultures of S. aureus, Pseudomonas and S. epider. were isolated; the S. aureus was noted to be resistant to all antibiotics. During the first month following the injury, the infection was not controlled by antibiotic treatment, and began spreading into the soft tissues of the forefoot. Even though high forefoot amputations result in considerable compromise in ambulation and a high degree of disability, amputation of the forefoot well proximal to the infected area was recommended.

Treatment with above-described device 10 was initiated a month after the injury occurred. The dressing was changed twice daily; the foot was soaked for 15 minutes per day in a one-third dilution of commercial hydrogen peroxide. One week later, cultures of the wounds were negative, wound edema and redness had disappeared, and the patient began protected ambulation. Over the next month, the wounds healed well with normal, full-thickness skin with normal dermatoglyphic lines and full normal sensation. The patient thereafter resumed normal activity.

EXAMPLE 2

A 56-year-old female was fitted with a lower denture after extraction of several teeth. Shortly thereafter, open abrasions of portions of the mandibular gum due to underlying bone irregularities developed, accompanied by pain, irritation and swelling. A device 10 consisting of two layers of thin silver nylon material was applied over the mandibular ridge, positioned to cover the irritated and abraded areas. The denture was reinserted over device 10.

The patient reported complete cessation of pain within 10 minutes. She wore the denture continuously for approximately 8 hours following application of the device 10. When the denture and device 10 were removed, the gum was pain-free and appeared normal. The patient was able to insert the denture on the following day without difficulty; she has experienced no further pain, discomfort or swelling in the area.

If desired, device 10 may include additional layers of materials deemed to have useful properties, including but not limited to absorbent and adhesive materials. For example, an absorbent layer 24 may be placed between sheets 18a, 18b (Fig. 3B), and/or an additional absorbent layer 26 between layers 14, 18a (Fig. 3C). Layers 14, 24, 26, if present, are soft,

flexible, moisture-absorbing materials as described above. Layers 14, 24, 26 need be no more than approximately 0.1–0.5 cm thick for most applications; however, thicker layers may be useful when device 10 is used in the care of relatively large draining wounds.

Another treatment device 40 according to the present invention is shown in Figs. 5A and 5B. Device 40 is a multilayer wound packing material that includes at least one layer with an antimicrobial metal such as silver. Device 40 preferably includes at least two layers 42, 44 of thin, flexible, conformable, wettable, silver-containing fabric such as that described above for layers 18a, 18b of device 10. Layers 42, 44 need be no more than approximately 1–2 mm thick for most applications; however, thicker layers may be useful when packing material 10 is used in the care of draining wounds.

In a preferred embodiment of the present invention, layers 42, 44 are made of a flexible, conformable, absorbent material that contains at least approximately 2 wt.% silver, more preferably at least approximately 10–15 wt.% silver. The material is dimensionally stable and easily handled, whether wet or dry. Layers 42, 44 may be made by weaving, knitting, felting, blowing, or other convenient process, and consist of silver-coated or silver-impregnated fibers. Suitable materials include felted ("pile") silver nylon, "matted" silver nylon, loop, and warp knit silver nylon fabrics made by Omnishield, Inc.; silver-impregnated fabrics made by Swift, Inc., Sauquoit Industries and other manufacturers may also be useful for the practice of the invention.

Device 40 may include additional layers of materials deemed to be useful in wound packing applications, including not limited to one or more layers 46 of absorbent material (Fig. 5B). Layer (or layers) 46, like layers 42, 44, is flexible and conformable. Layer 46, if present, is a soft, flexible, moisture-absorbing material such as woven or nonwoven cotton, absorbent polyester, etc. Layer 46 need be no more than approximately 0.1–0.5 cm thick for most applications; however, thicker layers may be useful when device 40 is used in the care of draining wounds. Alternatively, device 40 may include a layer of substantially moisture-impermeable material that, if present, helps direct fluids to layers 42, 44.

The layers of device 40 are bonded together at their outer edges by any convenient technique, including but not limited to crimping, embossing, application of heat and/or pressure via heated rollers, and biocompatible adhesives (Fig. 6A shows a 2-layer device 40 with crimped edges 48a, 48b). Techniques such as heat/pressure bonding are preferred, since these avoid the use of additional materials such as adhesives, fixatives, and so forth.

Like above-described layers 18a, 18b, layers 42, 44 consist of a dimensionally stable, biologically inert, easily handled and substantially non-adhering substrate to which silver (or some other metal with medically useful properties) has been added by any convenient technique known in the art. Individual fibers or microfibers can be coated and then worked (woven, knitted, crocheted, felted, blown, etc.) into a fabric; alternatively, silver may be added to the finished fabric. Suitable substrate materials include those listed above for layers 14, 18a, 18b, made by weaving, knitting, felting, blowing, or other process.

Layers 42, 44 contain at least approximately 2 wt.% silver (or other metal with useful antimicrobial properties), more preferably, at least approximately 5–10 wt.% silver. Individual fibers can be coated and then worked into a fabric; alternatively, silver may be added to the finished fabric. The wt.% silver, specific resistance and conductivity, the proportion of silver-containing fibers to plain (i.e., not containing silver) fibers, and other properties (fiber basis weight, shape, manufacturing technique) of useful fabrics may vary broadly. Materials containing less metal may be useful for some applications, as may those with higher specific resistances. However, it should be understood that the materials for layers 42, 44 are selected with a view to providing the needed amounts of free silver to the treatment site. When device 40 is placed in contact with body tissues and moistened by a suitable liquid, the silver in layers 42, 44 releases silver ions by the passive dissolution from the metallic silver surface so that, over a period of time, at least a portion of the available silver migrates to the immediately-adjacent tissues where it has useful antimicrobial, antifungal and antiviral effects.

Upon placement on or in a wound, silver ions are released from device 40 into the immediately-surrounding region. The rate of release generally rises to a maximum that depends on the silver content of material 10, then gradually decreases over a period of approximately 12–72 hours. As each silver ion leaves the fabric substrate of layers 42, 44, it is replaced by an ion from the local wound environment (i.e., chloride, etc.). In addition, some of these other ions bind spontaneously to the silver crystals remaining on the fabric. Thus, while layers 42, 44 may still contain silver at the end of several treatment periods, at least some of that silver will be unavailable for treatment purposes.

Useful antimicrobial effects obtained with a device according to the present invention tend to occur approximately 12–24 hours after placement. Thus, devices 10, 40 are changed at least daily, and preferably at least twice daily. Devices 10, 40 may be washed and reused, particularly under field conditions, provision of fresh dressings is preferred.

Device 40 may be used in the same manner as conventional wound packing materials. As illustrated by the following non-limiting example, a treatment device according to the present invention is especially useful in the care of antibiotic-resistant infections.

EXAMPLE 3

A 71-year-old male construction worker (retired, insulin-dependent diabetic) developed an infection of the right foot at the 1st MAP joint which penetrated to the bone. Despite treatment with multiple antibiotics, the infection progressed into the entire foot and a below-knee amputation was required. Two years afterwards, the patient developed a similar infection on his left foot. Despite treatment with multiple antibiotics, the infection progressed into the first metatarsal. The patient was referred to an orthopedic surgeon for a below-knee amputation on the left foot. Due to his age and general physical condition, the patient would in all probability have been unable to ambulate with two lower leg prostheses.

Examination confirmed the existence of an adequate dorsal incision over the first inter-metatarsal space with visible bone (1st and 2nd metatarsals). The head of the 1st metatarsal had been partially destroyed by the infection and the medullary cavity was open and draining. The patient's diabetes was uncontrolled due to the failure of multiple antibiotics and surgical treatment (incision and drainage) to control the infection. The area was markedly edematous, intensely reddened due to infection and irritation, and there was profuse drainage from the wound. Nerve sensation was totally absent over the involved area. Cultures showed the presence of Staph. aureus, Enterobacter. cloacae and an unidentified streptococcus.

The cavity extended proximally along the first metatarsal with the most proximal area proximal to the surgical incision. The cavity was irregular in internal contour and required multiple strips of device 40 (in the form of 3 mm wide strips cut to approximately 5 cm lengths) for complete packing. The packed wound was covered with a dressing in the form of a 3" square (about 7.6 cm square) device 10. All packing and dressing components (i.e., devices 10, 40) were changed at 24-hour intervals. The cavity was irrigated with a 30% hydrogen peroxide solution between changes.

By the end of the first week of treatment, cultures revealed far fewer microorganisms and the patient's diabetes was well under control. By the end of the second week, the wound was clean. Packing with device 40 continued (lesser amounts were needed as the wound healed from the inside up). Healing was complete by the end of the sixth week, with normal full-thickness, fully-innervated skin. The area was not painful, and the patient was able to bear full weight and ambulate will with the below-knee prosthesis on his other leg.

EXAMPLE 4

A 72-year-old male underwent extraction of two lower teeth (#'s R2 and R3) under local anesthesia (mandibular nerve block). Immediately following extraction, a suitable quantity of device 40 (in the form of a 2 mm wide strip) was packed into the extraction site and covered with several gauze pads. Approximately 30 minutes following extraction, the mandibular nerve block began to wear off and sensation returned to the area. The post-anesthetic pain usually felt following a nerve block did not occur. The patient reported slight discomfort at the extraction site at that time, which was self-treated with an over-the-counter analgesic.

Within 1–1/2 hours following the extraction, the site and surrounding area were pain-free. At that time, the initial dressing was carefully removed to avoid disturbing the blood clot in the extraction sockets. A smaller amount of device 40 was then carefully inserted into the cavity and covered with device 10 (in the form of a 3 cm square pad), covered with a few 2.5 cm square gauze pads as a bite block. This combination dressing was kept in place for an additional 3 hours. The patient experienced no bleeding at the extraction site.

On the first and second post-operative days, fresh dressings (device 40) were applied to the extraction site and kept in place for several hours. Forty-eight hours following the

extractions, the patient had been treated for a total of 11 hours and the wound appeared to be filling in with granulation tissue. Seventy-two hours following the extractions, the wound was closed with normal gum tissue.

Device 40 may be furnished in dimensions to suit a variety of applications, for example, 1–2" (about 2.5–5.0 cm) widths that can be cut to any needed length for covering surgical incisions and relatively small wounds. Wider devices 40 can be provided for covering large wounds such as burns and abrasions, and smaller, individually-packaged devices for small incisions, cuts, etc. Narrow strips (approximately 1–5 mm wide) may be useful for packing incisions, cavities, dental extraction sites, etc. If desired, device 40 can be covered by an appropriately-sized device 10 or other suitable dressing when in use. The device can be packaged in a dispenser 50 (Fig. 6B), encased in paper or plastic to help maintain sterility prior to use, or delivered to the end user in any other convenient form.

A device 40 according to the present invention provides prophylactic and/or therapeutic activity to help prevent (or treat) infection, provide anti-inflammatory and anti-allogenic effects, promote healing and, in some cases, also provide local analgesia. When used as a wound packing material, device 40 is flexible and conformable to the area to be treated. The optimum dimensions and configurations of the device depend on the size and location of the area to be treated.

The incidence rate of post-surgical infections in U.S. hospitals typically approaches 5%–15%; many of these infections are highly resistant to antibiotics. A device according to the present invention can be used as a packing material, or applied immediately post-surgery after removal of all chemical skin disinfectants. Such a dressing is believed to provide a high degree of prophylaxis for post-operative infections. Importantly, while devices 10, 40 have significant bactericidal, anti-inflammatory, and anti-allogenic effects in the treated area, there are no systemic effects and no entry of silver ions into the circulatory system.

In use, device 40 is applied to the treatment site after appropriate preparation (débridement, irrigation, etc.). Depending on the area to be treated, device 40 may be moistened to promote the release of silver, which migrates into the treated area to minimize external and cross-contamination of the treatment site and help prevent bacterial and fungal infections, while not hindering normal cell growth or repair. No toxic substance is introduced into the patient's body. Like above-described device 10, device 40 is preferably replaced at intervals of approximately 12–24 hours; however, the device may safely left in place for longer periods of time if circumstances so require (for example, under field conditions). It should be noted that device 40 is self-sterilizing, that is, the silver-containing fabric of layers 42, 44 sterilizes itself in water. Therefore, while application of a fresh, unused device 40 every 12–24 hours is recommended, a patient can rinse and reuse the device, or leave it in place for several days, under emergency conditions.

As noted above, at least some of the odor due to perspiration and other body secretions, including locker-room odor, is due to odor-causing bacteria (including

Brevibacterium epidermidis, Corynebacterium xerosis, Micrococcus lylae, and Staphylococcus epidermidis) and other microorganisms which are normally present on the skin. Resident populations of these bacteria can be reduced by cleansing the skin. However, the odor returns as the remaining bacteria quickly multiply in the relatively warm, relatively moist environment of the armpits, shod feet, etc. Antiperspirants reduce perspiration, which serves as a growth medium for bacteria, fungi, etc.; with a lesser amount of perspiration to serve as a growth medium, these microorganisms multiply more slowly, so the onset of perceptible odor after washing is delayed. However, antiperspirants have little if any effect on locker-room odor.

Referring now to Fig. 7A, there is shown an antimicrobial device 60 according to the present invention. In its simplest embodiment, device 60 consists of a single sheet of fabric such as above-described sheet 18 (or sheets 42, 44) that contains sufficient silver or other bactericidal metal to provide beneficial antimicrobial effects. Sheet 18 is flexible, conformable, nonadhering to intact skin and exposed tissues, and contains at least approximately 5 wt.% silver (however, fabrics with lower silver contents may also be useful). More preferably, sheet 18 contains at least approximately 10 wt.% or more silver.

Device 60 may include at least two sheets 18a, 18b of such a fabric, as shown in Fig. 7B. If desired, one or both of sheets 18a, 18b may be at least somewhat moisture-absorbent. Sheets 18a, 18b need be no more than approximately 1–2 mm thick; however, thinner or thicker sheets may be also be useful. Sheets 18a, 18b are bonded together at edges 62a, 62b by any convenient technique, including but not limited to crimping, embossing, application of heat and/or pressure via heated rollers. Biocompatible adhesives, while not preferred, may also be useful for the practice of the invention. Techniques such as heat/pressure bonding are preferred, since these avoid the use of additional materials such as adhesives, fixatives, and so forth.

Device 60 may include additional layers of materials deemed to be useful, including not limited to a sheet 64 of absorbent material and/or a moisture-impermeable material that serves as an occlusive barrier (Fig. 7C). Sheet 64, like sheets 18a, 18b, is flexible and conformable, preferably a soft, flexible, moisture-absorbing material such as woven or nonwoven cotton, absorbent polyester, etc. Sheet 64 need be no more than approximately 0.5–2.0 mm thick for most applications. The edges of sheet 64 may be attached to the edges of sheets 18a, 18b by any convenient technique, including but not limited to sewing, crimping, embossing, application of heat and/or pressure via heated rollers, and biocompatible adhesives. Alternatively, sheet 64 may be a substantially moisture-impermeable material that acts as an occlusive barrier to entrain moisture (including perspiration) and direct it towards the target.

As described in the following non-limiting example, a device 60 is simply placed inside a sock, stump sock or liner, or shoe for use.

EXAMPLE 5

Thermoplastic stump socks or liners are closely-fitting to provide good cushioning, reduction of chafing and skin irritation, and reduction of air pocket formation which leads to undesirable pistoning effects. However, these types of liners also provide a hospitable environment for the growth of odor-causing bacteria: users report pronounced "dirty sock" or locker-room type odors after even a few hours' use.

A volunteer subject placed a 1" (about 2.5 cm) square device 60 into the bottom of a form-fitting thermoplastic stump sock worn as a liner with his conventional below-knee prosthesis. The liner and prosthesis were worn for a full day (approximately 14 hours). The subject reported no perceptible odor upon removal of the liner and prosthesis at the end of the day. In contrast, he routinely noticed a strong locker-room type odor after wearing the prosthesis and stump sock without device 60.

Device 60 is small, thin, light in weight, flexible and conformable, so it does not interfere with the fit of the user's normal footgear (socks, shoes, etc.). Device 60 is inert until wetted by perspiration, other body fluid, or indeed any of a variety of fluids including water. Then, the bonds between the silver atoms and the fabric substrate are loosened and at least some free silver ions are released from the fabric of sheets 18a, 18b and act to inhibit the growth of microorganisms in the region, including at least some of the bacteria believed to cause objectionable locker-room type odors. The rate of release depends on factors that include the silver content of sheets 18a, 18b and the amount of moisture present.

Device 60 may be furnished in any convenient dimensions, for example, 1–2" (about 2.5–5.0 cm) squares, or strips that can be cut to size for each individual user. The device can be packaged in a dispenser, encased in paper or plastic to help maintain its integrity prior to use, or be delivered to the end user in any other convenient form.

An antimicrobial device 60 according to the present invention reduces odor by slowing the growth of odor-causing microorganisms, thereby enhancing the user's comfort and self-esteem. Device 60 is essentially imperceptible to the user when worn inside socks (including stump socks) or stockings, or inside shoes, boots, or sneakers. Importantly, device 60 has no systemic effects, and its use does not result in entry of silver ions into the circulatory system. Use of device 60 does not lead to the development of either localized or systemic argyria.

An antimicrobial treatment device according to the present invention can be made in a variety of configurations adapted to the intended use. Additional embodiments of the invention are shown in Figs. 8A and 8B. An iontophoretic treatment device 80 (Fig. 8A) has a first, electrically nonconductive outer layer 12, a second, intermediate layer 14, a inner layer with at least two sheets 18a, 18b, and, optionally, an edge adhesive 20 as described above for device 10. A snap-type connector 82 extends through layer 12 and makes electrical contact with layers 18a, 18b. Connector 82 is silver (or silver-plated). Applying current at the

central connector 82 ensures an approximately uniform current distribution at the treatment site.

Device 80 can be made in a variety of sizes, for example discs approximately 1–6" (about 2.5–15 cm) in diameter. For use as an anode in iontophoretic treatment, device 80 is large enough that adhesive 20 (if present) does not contact the wound.

A return electrode 100 includes an outer layer 12, a layer 14, edge adhesive 20, and an electrical connector 102, generally as shown in Fig. 8B. Layer 14 is made of any suitable low-resistance material for making good electrical contact with intact skin. For example, layer 14 may be a relatively thick (at least 3 mm) material with a silver content of at least approximately 10 wt.% (preferably at least approximately 15 wt.%). Alternatively, low-resistance, electrically-conductive thermoplastic materials may also be useful. As for above-described device 10, the inner sides of devices 90, 100 are protected with removable strips of material (not shown) that are peeled off just prior to use.

Layer 14 of return electrode 100 is preferably made of a material that does not include chopped fibers. Many "matted"-type materials are made of chopped fibers that are compressed into a mat. If these types of materials are used in wound dressings, particularly on open wounds, there is a possibility that small fiber fragments will become separated from the main fabric mass and be retained in the wound. Suitable materials for layer 14 of devices 90, 100 (and layers 18a, 18b, 42, 44 of above-described devices 10, 40, 50) include those made of small-diameter nylon microfibers that are spun into a single thread that is then silvered. Such materials can have an electrical resistance as low as approximately 0.5 Ω/cm.

Other low-resistance materials are also suitable for use with the invention. For example, silver-containing thermoplastic materials such as those manufactured by the Chomerics Division of Parker Hannifin Corp. of Woburn, MA have resistances as low as 0.1 Ω/5 cm. The use of low-resistance materials for layer 14 of devices 90, 100, results in decreased total circuit resistance at the point of skin contact, resulting in increased total circuit current and increased silver ion output. It is believed that use of lower-resistance materials for layers 18a, 18b of device 10, layers 42, 44 of device 40, and layers 48a, 48b of device 50 may also result in increased silver ion output.

In use, devices 80, 100 are suitably positioned and secured to the patient's body, then connected to a power source to provide the desired iontophoretic treatment. Both devices can be made in any desired size and shape for a variety of applications.

Additional treatment devices according to the present invention are shown in Figs. 9A–C. A multilayer treatment device 120 has a thin, flexible outer layer 12, an intermediate layer 122, and at least one inner layer 18 of silver-containing fabric as described above (Fig. 9A). Layers 12 and 122 are preferably made of a thermoplastic material that softens when exposed to heat and returns to its original condition when cooled to room temperature.

Suitable materials include polyvinyl chloride, nylon, fluorocarbon compounds, polyethylene, polyurethane, polystyrene, polypropylene, and various cellulosic and acrylic resins.

Layer 122 has a plurality of throughholes 124 arranged in any convenient pattern. A sponge 126 is inserted in each throughhole 124, so that sponges 126 contact silver-containing layer 18. Sponges 126 are made of a soft, flexible and conformable, moisture-absorbing material, including but not limited to cotton, polyester, rayon, dacron, polyurethane, polypropylene, acrylics and modacrylics, polyvinyl acetate or other synthetic materials, or combinations thereof, in woven, nonwoven, foam, or sponge-like form. Layer 122 and sponges 126 need be no more than a few millimeters thick for most applications. Sponges 126 are wetted to provide a moisture reservoir for silver-containing layer 18 when device 120 is in use.

The edges of layers 12, 18, and 122 may be attached together by any convenient technique, including but not limited to application of heat and pressure, embossing, crimping, sonic welding, needle punching, and biocompatible adhesives such as above-described adhesive 16. However, techniques which avoid the use of adhesives, fixatives, and so forth are preferred.

Another device 140 has layers 12, 18, and 122 (with sponge inserts 126) as described above for device 120 (Figs. 9B and 9C). A groove 142 is formed near a perimeter 144 of sheet 122, and a corresponding rib 146 near a perimeter 148 of sheet 12. Groove 142 and rib 146 form a fastener 150 that allows the user to wholly or partly remove outer layer 12 from device 140, for example, to add additional water or other liquid to sponges 126 so as to maintain an effective moisture reservoir for silver-containing layer 18. Layer 12 can easily be replaced simply by pushing rib 146 back into groove 142.

An antimicrobial treatment device according to the present invention provides prophylactic and/or therapeutic activity to help prevent (or treat) infection, provide anti-inflammatory and anti-allogenic effects, and promote healing. Importantly, while the device has significant bactericidal, anti-inflammatory, and anti-allogenic effects in the treated area, there are no systemic effects and no entry of silver ions into the circulatory system. The optimum content of silver (or other useful metal) depends on the particular application; thus, fabrics with silver contents outside the above-quoted ranges may also be useful for the practice of the invention.

The device is flexible and conformable to the area to be treated. When used as a wound treatment device or wound packing material, the optimum dimensions and configurations of the device depend on the size and location of the area to be treated, and include considerations of affixing the device in place, controlling moisture loss from the wound, and ensuring direct contact between the silver-containing material and the actual wound surface itself. In use, a device 10 (or device 40) is applied to the patient's skin after appropriate surface preparation (the devices are preferably applied to dry skin so that adhesive 20 adheres well to the skin to hold the device in place). Depending on the area to be treated,

layer 14 may be moistened to promote the release of silver, which minimizes external and cross-contamination of the treatment site and helps prevent bacterial and fungal infections, while not hindering normal cell growth or repair. No toxic substance is introduced into the patient's body. Devices 10, 40 are preferably replaced at intervals of approximately 12–24 hours; however, the devices may safely left in place for longer periods if circumstances so require (the devices may even be rinsed and reused if necessary, for example, under field conditions) A device according to the invention can be used for prophylactic treatment of fresh wounds and surgical incisions, treatment or prevention of early stage decubital ulcers ("bed sores"), therapeutic treatment of infected and traumatic wounds, and so forth.

As noted above, use of two silver-containing sheets such as 18a, 18b is based on the surprising discovery that a treatment device with two or more silver-containing sheets is more effective than one with a single such sheet due to improved silver ion migration resulting in enhanced therapeutic effects. Even though only one of the two sheets typically contacts the treatment site, two sheets provide at least the same amount of silver ions at the site as a single sheet having twice the silver content. This property results in an device that delivers more silver, without the disadvantages of powdering and flaking associated with fabrics having higher silver contents.

As a delivery system for silver, a fabric with a sufficiently high concentration of silver releases silver ions at a steady rate for as long as the fabric is in contact with the culture medium (in vitro or in vivo). Such fabrics are not known to cause allergic reactions, thus, their use prevents some of the potentially-harmful side effects associated with other silver delivery systems (silver sulfadiazine, silver thiosulfate). Devices that incorporate such fabrics are nonhazardous, conformable to the shape of the site to be treated, readily adaptable to diverse clinical situations, and safe and easy to use. When treating patients with extensive burns, a device according to the invention is less expensive, less cumbersome, and more effective than silver sulfadiazine cream.

With respect to the above description of the invention, it is to be realized that the optimum dimensional relationships for the parts of the invention, to include variations in size, materials, shape, form, function and manner of operation, assembly and use, are deemed readily apparent and obvious to one skilled in the art, and all equivalent relationships to those illustrated in the drawings and described in the specification are intended to be encompassed by the present invention. Therefore, the foregoing description is considered as illustrative only of the principles of the invention. Further, since numerous modifications and changes will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation shown and described, and accordingly, all suitable modifications and equivalents may be resorted to, falling within the scope of the invention. Thus, it will be apparent to those skilled in the art that many changes and substitutions can be made to the preferred embodiment herein described without departing from the spirit and scope of the present invention as defined by the appended claims.

WHAT IS CLAIMED IS:

1. A device for slowing the growth of microorganisms in vivo, said device comprising:

a first layer; and

at least one second layer engaging a side of said first layer, at least one of said first and second layers carrying a quantity of a bactericidal metal.

2. The device as recited in claim 1, wherein said at least one layer contains at least approximately 2 wt.% of said bactericidal metal.

3. The device as recited in claim 1, wherein each of said first and second layers contains at least approximately 2 wt.% of said bactericidal metal.

4. The device as recited in claim 1, wherein each of said first and second layers contains approximately the same wt.% of said bactericidal metal.

5. The device as recited in claim 1, wherein at least a portion of said bactericidal metal is silver.

6. The device as recited in claim 1, wherein at least a portion of said bactericidal metal is crystalline silver.

7. The device as recited in claim 1, wherein said bactericidal metal is in a mechanically stable form.

8. The device as recited in claim 1, wherein said bactericidal metal further comprises silver, said silver mechanically attached said at least one layer so that, when said at least one layer is wetted, at least a portion of said silver is released in the form of ionic silver.

9. The device as recited in claim 1, wherein said first and second layers further comprises a fabric substrate carrying said bactericidal metal, said substrate made of a nonconducting, nonallergenic, non-adherent, mechanically stable material.

10. The device as recited in claim 1, wherein at least one of said first and second layers is made of a moisture-absorbing material.

11. The device as recited in claim 1, further comprising at least one absorbent layer, wherein one of said first and second layers engages a side of said absorbent layer.

12. The device as recited in claim 1, further comprising a substantially moisture-impermeable layer, wherein one of said first and second layers engages a side of said moisture-impermeable layer.

13. The device as recited in claim 12, wherein said moisture-impermeable layer is gas-permeable.

14. A treatment device for slowing the growth of microorganisms in vivo, said device comprising, in sequence:

an outer layer of substantially moisture-impermeable, electrically non-conducting material;

an intermediate layer of a moisture-absorbing material; and

an inner layer including at least two sheets of a bactericidal fabric.

15. The device as recited in claim 14, wherein said bactericidal fabric further comprises a fabric containing a bactericidal metal.

16. The device as recited in claim 14, wherein said bactericidal fabric further comprises a silver-containing fabric.

17. The device as recited in claim 14, wherein said bactericidal fabric contains crystalline silver.

18. The device as recited in claim 14, wherein said bactericidal fabric contains approximately 2–25 wt.% silver.

19. The device as recited in claim 14, wherein said intermediate layer contains approximately 2–25 wt.% silver.

20 The device as recited in claim 14, wherein said bactericidal fabric and said intermediate layer each contain at least approximately 2 wt.% silver.

21. The device as recited in claim 14, wherein said bactericidal fabric and said intermediate layer each contain at least approximately 2 wt.% silver, and wherein said bactericidal fabric has a higher wt.% silver content than said intermediate layer.

22. The device as recited in claim 14, wherein said bactericidal fabric and said intermediate layer each contain at least approximately 2 wt.% silver, and wherein said bactericidal fabric has a lower wt.% silver content than said intermediate layer.

23. The device as recited in claim 14, wherein said bactericidal fabric has a specific resistance no greater than approximately 5 Ω/cm.

24. The device as recited in claim 14, wherein said bactericidal fabric has a specific resistance no greater than approximately 1 Ω/cm.

25. The device as recited in claim 14, further comprising an adhesive layer attached to at least a portion of an inner side of said outer layer.

26. The device as recited in claim 14, further comprising means for connecting said bactericidal fabric to a source of electrical power.

27. The device as recited in claim 14, wherein said bactericidal fabric is a silver-containing nylon fabric.

28. The device as recited in claim 14, wherein said outer layer further comprises a thermoplastic material, and wherein said intermediate layer further comprises a layer of thermoplastic material carrying moisture reservoir means.

29. The device as recited in claim 14, further comprising user-operable means for removably attaching said outer layer to said intermediate layer.

30. A system for slowing the growth of microorganisms in vivo, said system comprising:

a sealed container; and

at least one antimicrobial treatment device in said container, said device including at least one fabric sheet carrying a quantity of a bactericidal metal.

31. The system as recited in claim 30, wherein at least a portion of said bactericidal metal is silver.

32. The system as recited in claim 30, wherein at least a portion of said bactericidal metal is crystalline silver.

33. The system as recited in claim 30, wherein said at least one fabric sheet contains at least approximately 2 wt.% said bactericidal metal.

34. The system as recited in claim 30, wherein said container and said device are presterilized.

35. The system as recited in claim 30, wherein said device further comprises:

a first fabric layer; and

at least one second fabric layer engaging a side of said first layer, at least one of said first and second layers carrying at least approximately 2 wt.% silver.

36. The system as recited in claim 30, wherein said device further comprises:

at least one absorbent layer;

at least one layer of nonconducting, non-adhering, nonallergenic fabric containing said bactericidal metal in mechanically stable form, said at least one fabric layer attached to said at least one absorbent layer.

37. The system as recited in claim 30, wherein said device further comprises:

an outer layer of substantially moisture-impermeable, electrically non-conducting material;

an intermediate layer of a moisture-absorbing material; and

an inner layer including at least one sheet of a bactericidal fabric.

38. The system as recited in claim 30, wherein said device further comprises:

an outer layer of substantially moisture-impermeable, gas-permeable, electrically non-conducting material;

an intermediate layer of moisture-absorbing material; and

an inner layer including at least one sheet of silver-containing nylon fabric.

39. A method for treating a wound, comprising:

providing a wound dressing having at least one layer carrying a quantity of a bactericidal metal; and

applying said dressing to a wound so that, when said at least one layer is contacted by wound exudate, at least a portion of said bactericidal metal is released in ionic form.

40. The method as recited in claim 39, wherein said applying step further comprises packing said dressing into said wound.

41. The method as recited in claim 39, wherein said applying step further comprises laying said dressing onto said wound.

42. The method as recited in claim 39, wherein said bactericidal metal further comprises silver, said silver mechanically attached to said at least one layer so that, when said at least one layer is wetted, at least a portion of said silver is released in the form of ionic silver.

43. The method as recited in claim 39, wherein said wound dressing further comprises:

at least one layer of a moisture-absorbing material; and

at least one layer of a bactericidal fabric, said bactericidal fabric containing silver.

44. The method as recited in claim 39, wherein said wound dressing further comprises:

an outer layer of substantially moisture-impermeable, electrically non-conducting material;

an intermediate layer of a moisture-absorbing material; and

an inner layer including at least two sheets of silver-containing fabric.

45. The method as recited in claim 39, further comprising the step of pre-moistening said dressing before applying said dressing to said wound.

46. The method as recited in claim 39, further comprising the step of changing said dressing at least approximately every twenty-four hours.

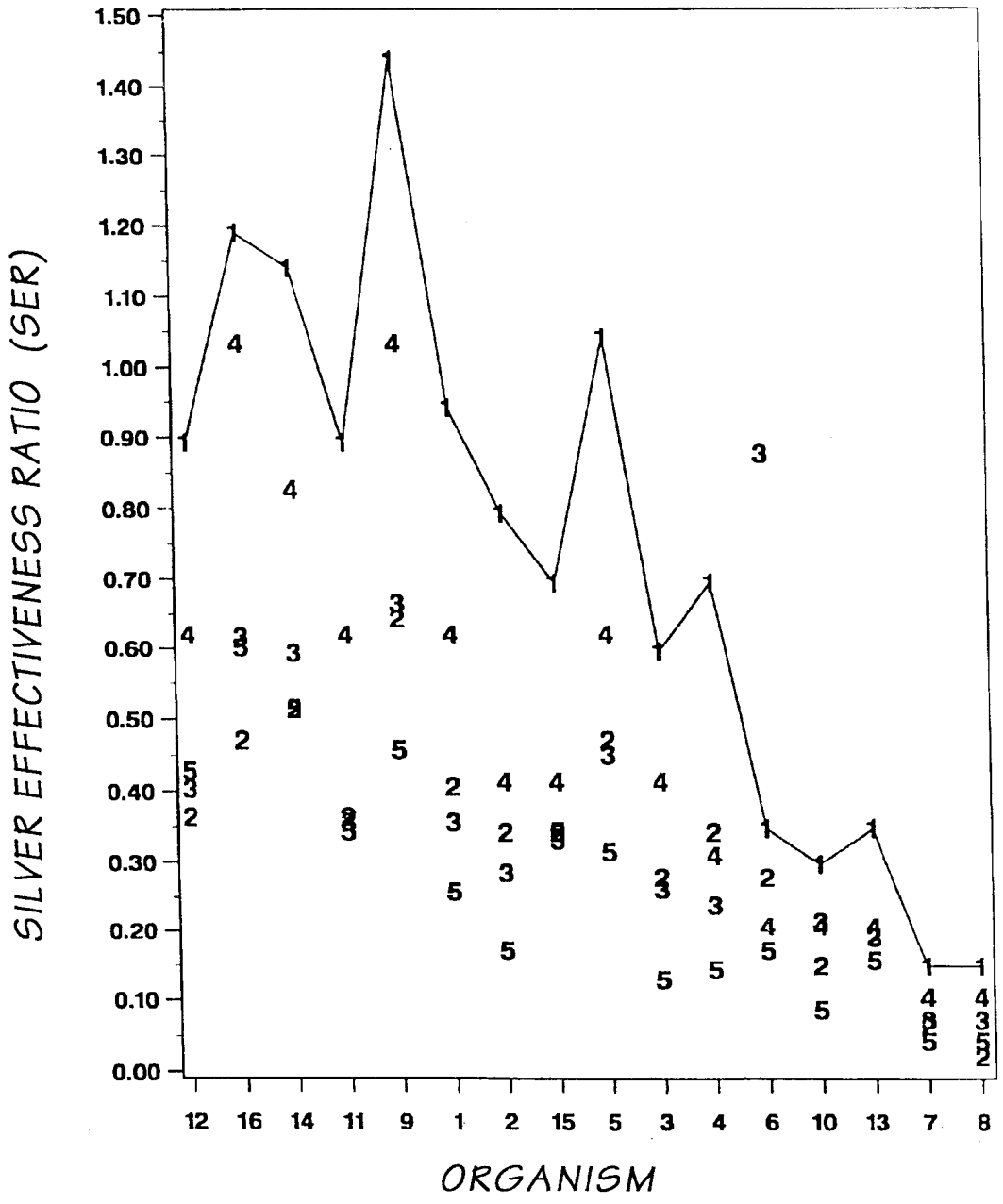
47. The method as recited in claim 39, further comprising the step of adding additional liquid to said moisture-absorbing layer.

48. A method for slowing the growth of odor-causing microorganisms in vivo, comprising placing a device inside an item of clothing so that said device contacts the skin of a user, said device containing a quantity of a bactericidal metal so that, when said device is contacted by perspiration, at least some of said bactericidal metal is released in ionic form to retard growth of microorganisms.

49. The method as recited in claim 48, wherein said device further comprises at least one sheet of a non-conducting, non-adherent fabric substrate, said substrate carrying at least approximately 2 wt.% silver.

50. The method as recited in claim 48, wherein said device further comprises at least one sheet of a non-conducting, non-adherent nylon substrate, said substrate carrying at least approximately 2 wt.% silver.

51. the method as recited in claim 48, wherein said device further comprises at least two sheets of a non-conducting, non-adherent, nonallergenic substrate, said substrate carrying at least approximately 2 wt.% silver.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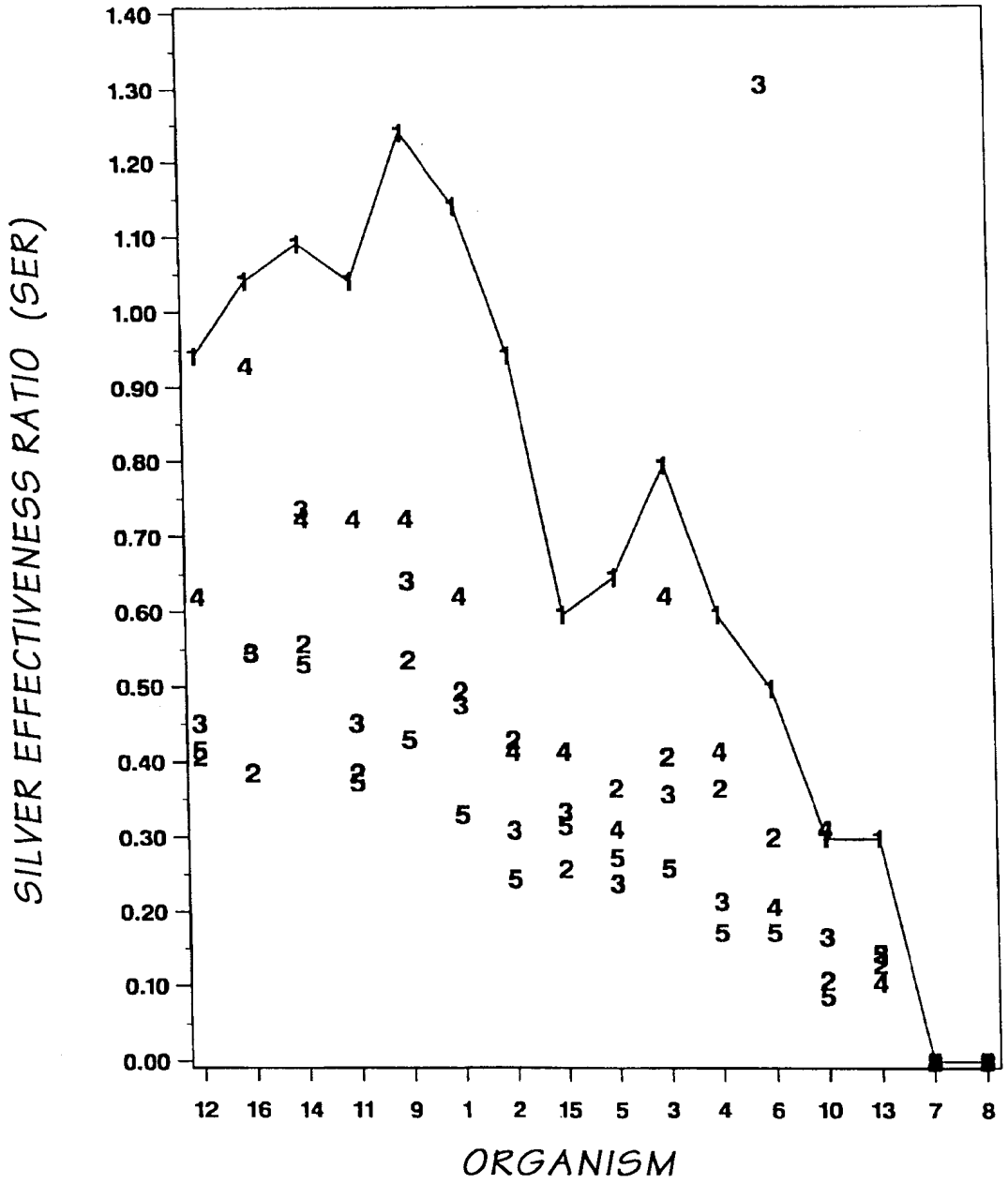
ORGANISM

Fig. 1A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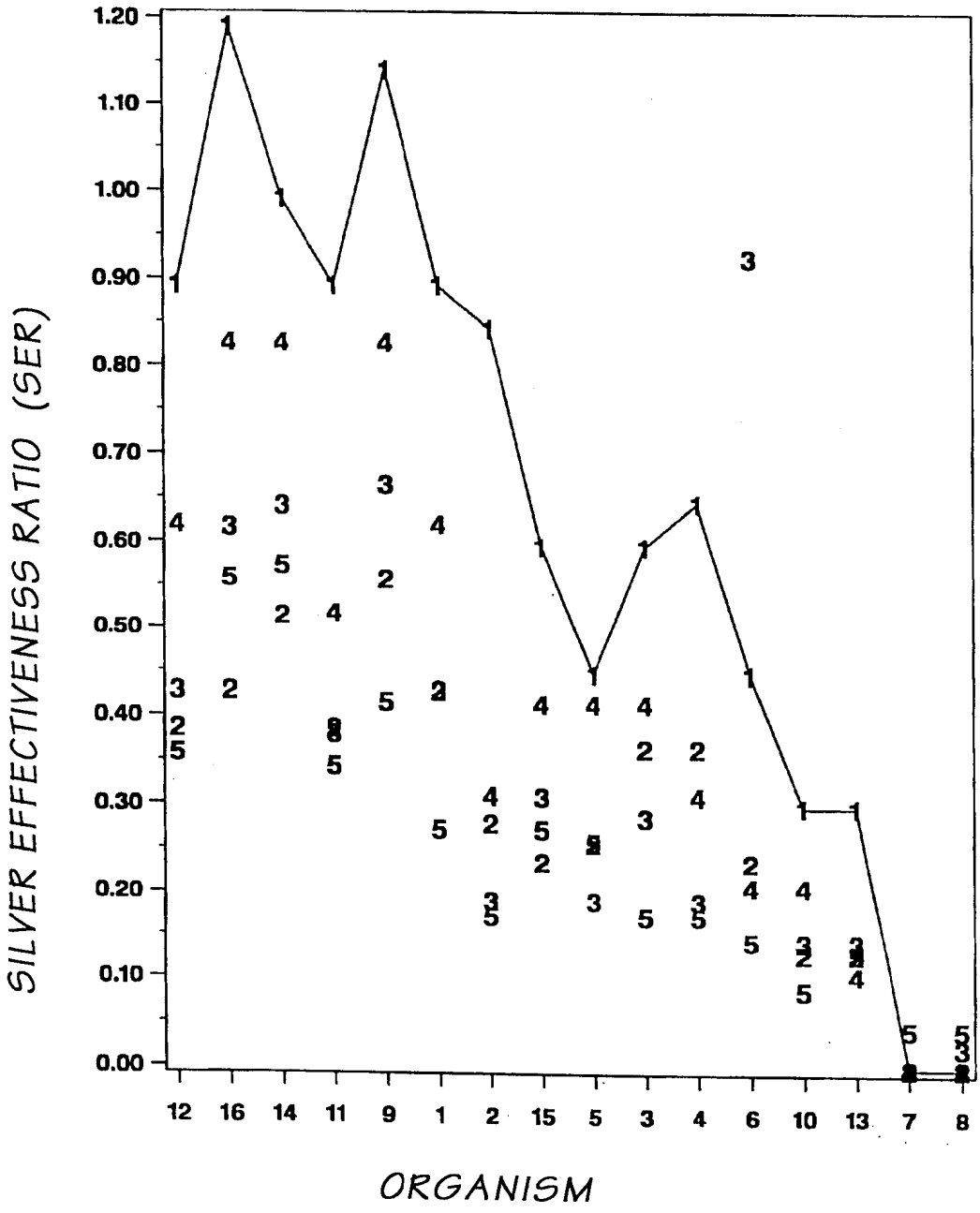
ORGANISM

Fig. 1B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ORGANISM

Fig. 1C

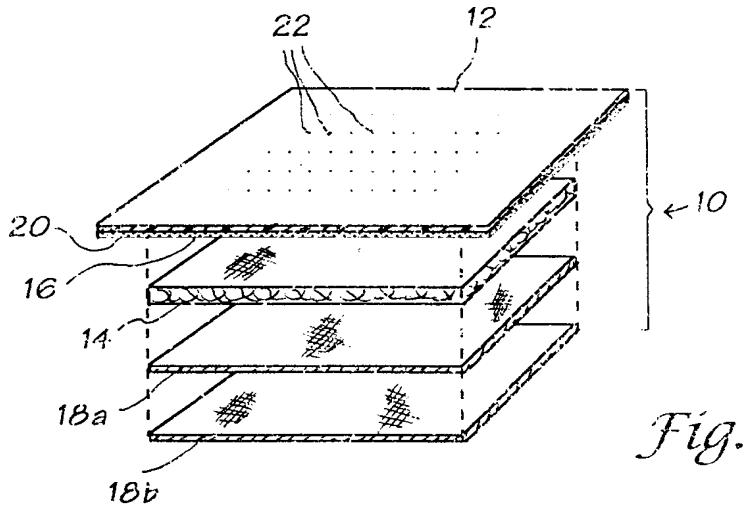

Fig. 2

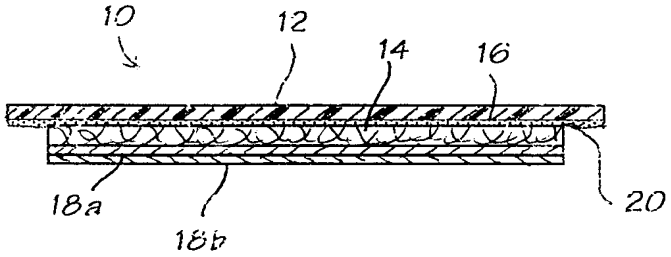

Fig. 3A

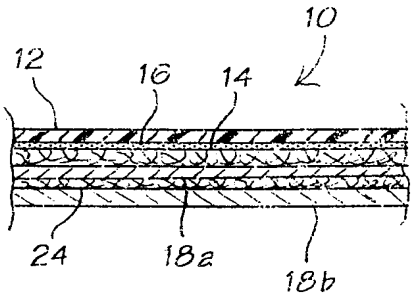

Fig. 3B

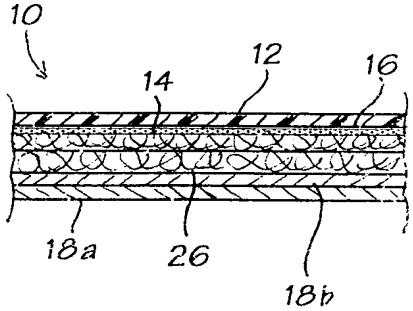

Fig. 3C

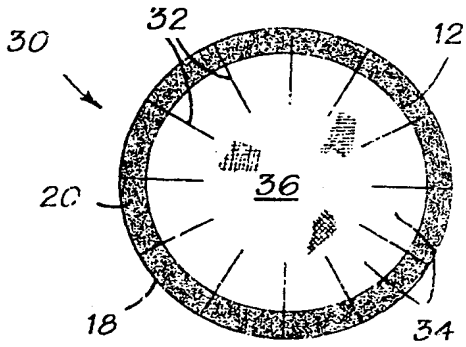

Fig. 4

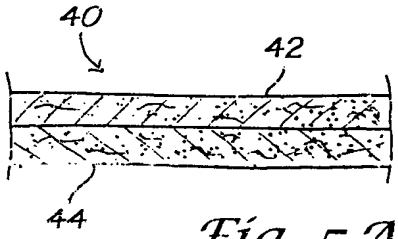

Fig. 5A

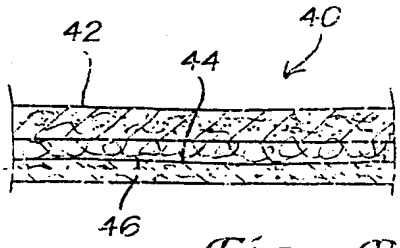

Fig. 5B

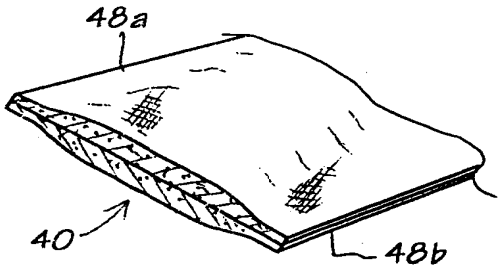

Fig. 6A

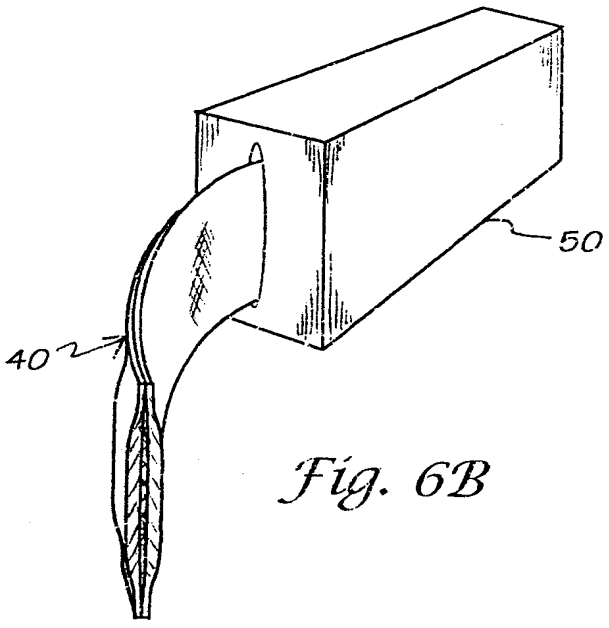

Fig. 6B

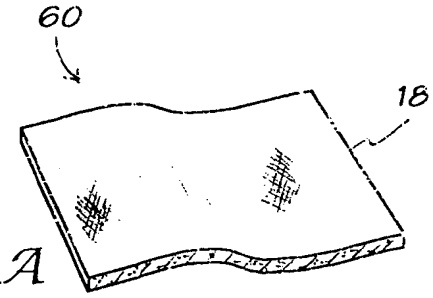

Fig. 7A

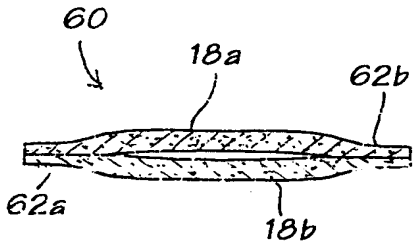

Fig. 7B

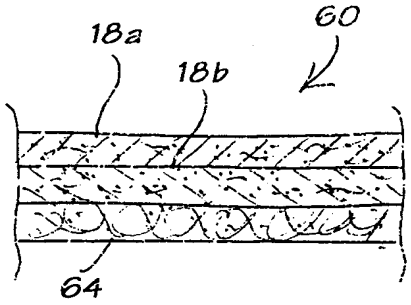

Fig. 7C

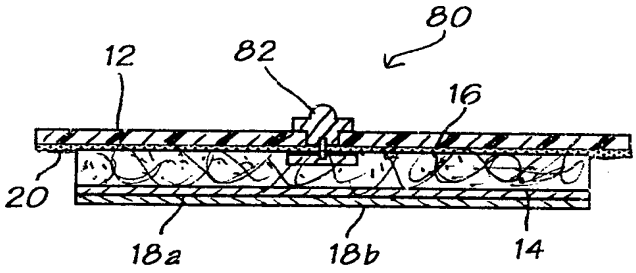

Fig. 8A

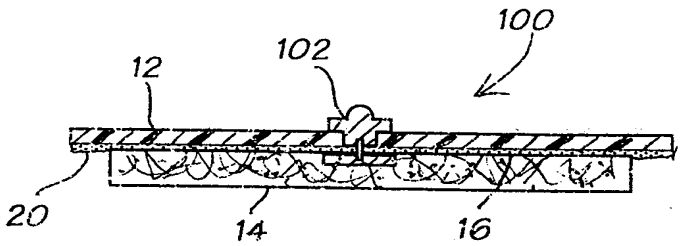

Fig. 8B

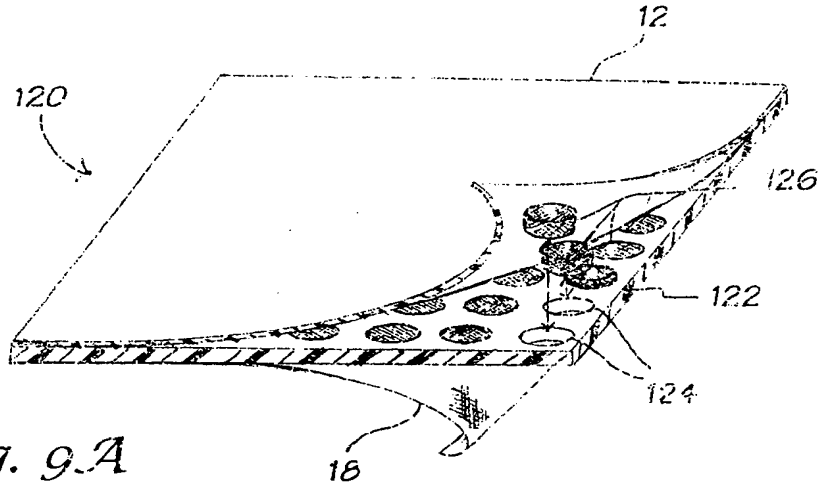

Fig. 9A

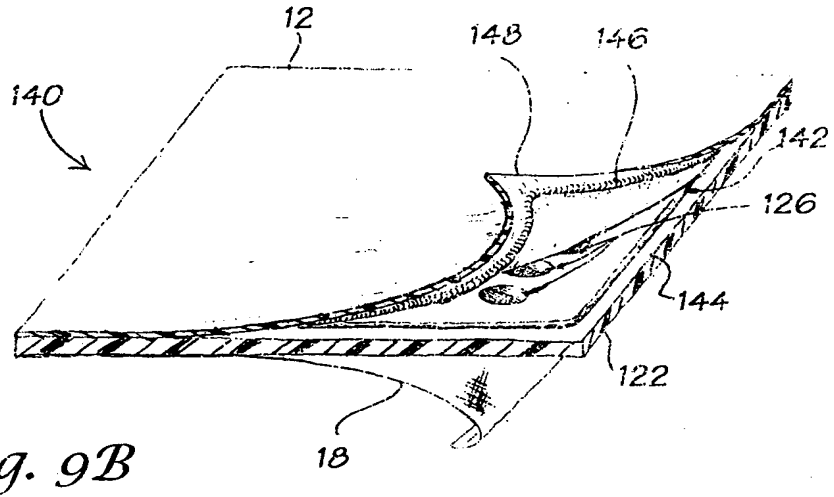

Fig. 9B

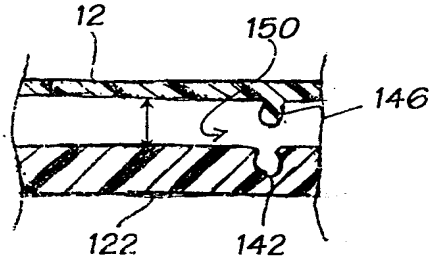

Fig. 9C